

FIG. 1

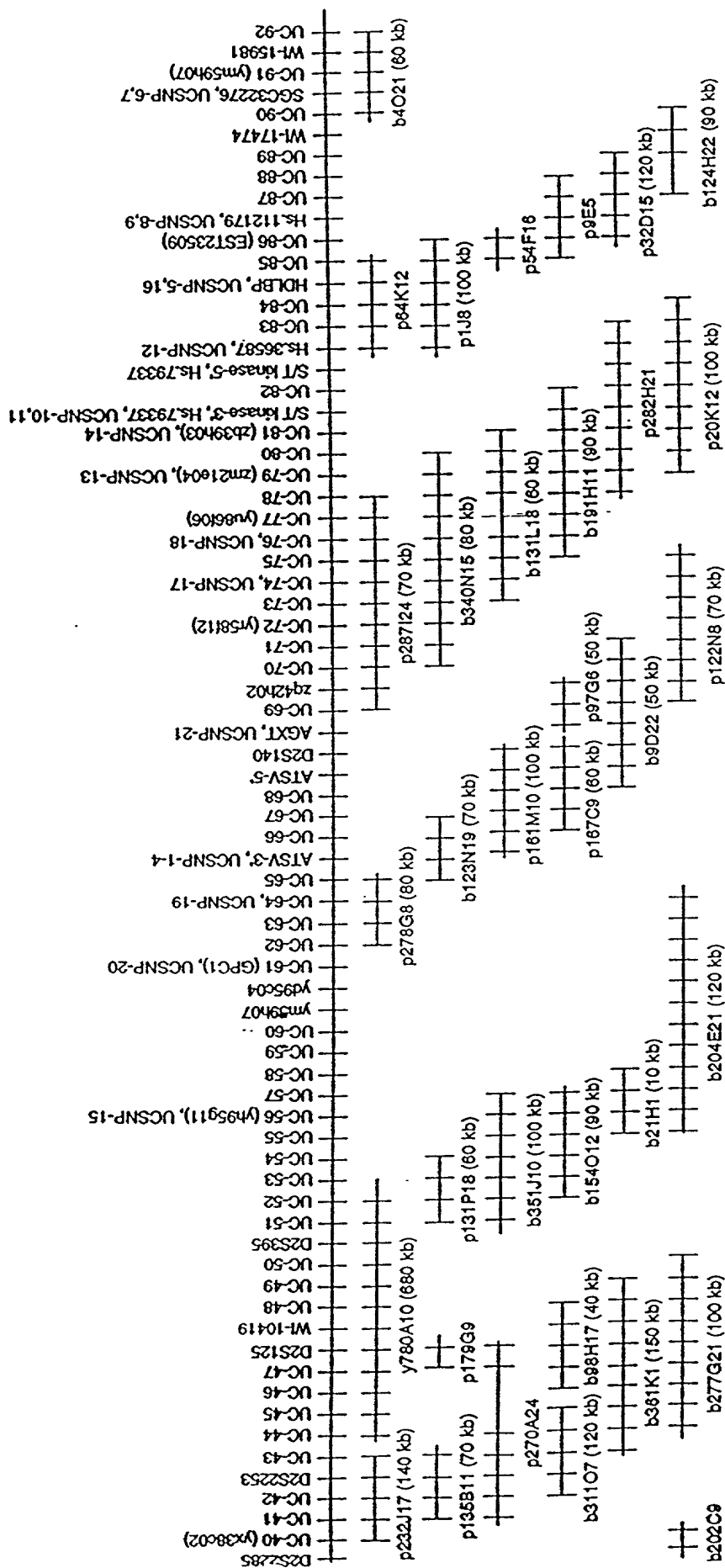


FIG. 2

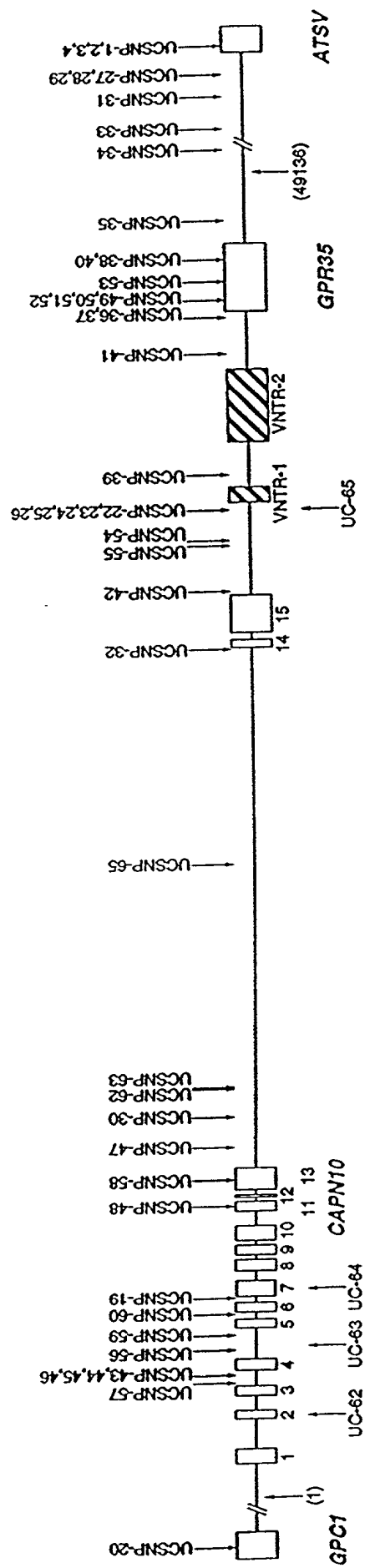


FIG. 3

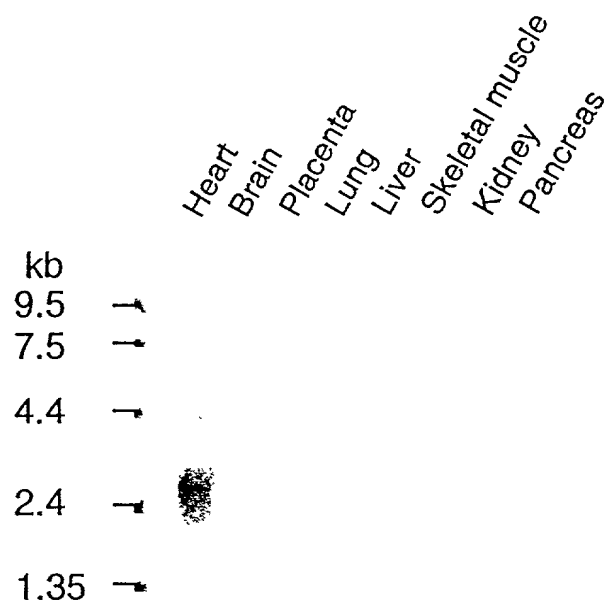


FIG. 4

		Domain I	Domain II	
hCAPN5	-----MFSCVKPYEDQNSALRQDCRRRKVLFDPLFPATDSDLYY-KGTGPG-----AVRWKRPKGCIEDPRLFVDG	67		
hCAPN6	-----MGPPILKLFKNQKYELQKQCKGDLFCDFTFLENDLFFNRLLEG-----KVWVKRPQDLSDDPHLIVGN	67		
hCAPN3	MPTVISASVAPRTAAEPRSGPVHPAQAQKATEAGGNGPSGYSALISRNPIIGVKEKTFEQLHKCKLEKVLVDPEFPDDETSLFYSQKFP-----IQFVWKRPEICENPRFIIDG	115		
hCAPN9	MPYLY-----RAPGPOAHVP-----KDARITHSSQSFQHRQECQLRGTLFEDADFPASNSSLFYSERPG-----IPFVWKRPEIKVKNPEFILGG	83		
hCAPN1	-----MSEEIITPVYCTGVSAQVQKQKARELGLG-----RHENAIIKYLQDQYDLRVRCLQSGTLFRDEAFPPVQSLGYKDLGPNSSKTYGKWKRPTELLSNPQFIVDG	101		
hCAPN2	-----HAGIAAKLAKDREAEGLG-----SHERAIIKYLQDYEALRNECLEAGTLFQDPSFPAIPALGFKELGYPSSKTRGHRKRPTEICADPQFIIG	91		
hCAPN8	-----HAALAGVSKQRAVAEGLG-----SNQNAVLYLQGDQFETLRRKQCLNSGVLFKDPFPCPSALGYKDLGPGSPDTQGIWVKRPTELCNPPQFIVGG	91		
hCAPN10	----------MRAGRGATPARELFRDAAPADSSLECDLSTPLAQFREDITWRRPQETCATPRLFPDD	59		
hCAPN5	ISSHDLHQGGVGNWVFAACSSSLASRESLWQKVIIPDKWQEWDPKCAQAYAGIFHFHFWRLG-HYDVVIDERLPTVNNQLIYCHSNRNEFWCALVEKAYAKLAGCYQALDGGNTADALV	186		
hCAPN6	ISNHQLIQGRGNKAMISAFSCSLAVQESHWTKAIPNKHQDQEWDPKPEYAGIFHFHFWHGEWTEVVDDLLPTINGDLVFSFSTSMNEFWALKEKAYAKLAGCYEALDGLTITTDIIM	187		
hCAPN3	ANRTDICQGGELGDCWFLAAIACLTINQHLLFRVIP-----HDQSFENYAGIFHFQFWRYGEWVDVDDCLPTVNNQLVFTKSNHNEFWALKEKAYAKLAGCYEALDGLTITTDIIM	229		
hCAPN9	ATRTDICQGGELGDCWLLAAIASLTINQKALRVIP-----QDQSEFGPYAGIFHFQFWHSEWLDVDDRLPTFRDLRVLFSADHNEFWALKEKAYAKLAGCYEALDGLTITTDIIM	197		
hCAPN1	ATRTDICQGGALGDCWLLAAIASLTINQKALRVIP-----HQQSFQNYAGIFHFQFWHSEWLDVDDLLPKDQGLVFSADHNEFWALKEKAYAKLAGCYEALDGLTITTDIIM	215		
hCAPN2	ATRTDICQGGALGDCWLLAAIASLTINQKALRVIP-----LQQSFQNYAGIFHFQFWHSEWLDVDDLLPKDQGLVFSADHNEFWALKEKAYAKLAGCYEALDGLTITTDIIM	205		
hCAPN8	ATRTDIRQGGGDCWLLAAIASLTINQKALRVIP-----RDQSFQKDYAGIFHFQFWHSEWLDVDDLLPKDQGLVFSADHNEFWALKEKAYAKLAGCYEALDGLTITTDIIM	205		
hCAPN10	PRDQGVQKGLGDCWFLCAACALQKSRHLLDQVIP-----PGQSWADQYRGSFTCRIVQFGRWVEVTTDDRLPCLAGRLCFSRQREDVFWLPLEKVIKHYGSEHLMAGQVADALV	175		
hCAPN5	DFTGGVSEPIDLTEGDFANDETKRNQLFERMLKVHSGGLISASIKAV-----TAADK-----EARLACGLVKGHAYAVTDV	258		
hCAPN6	DFTGTLAEIIDMQGRYTDLVEEKYKLFGLYKTFKGLICCSIESP-----SQEEQ-----EVETDGLKGYTYTMDI	259		
hCAPN3	DFTGGVAEFTIR-----APSDMYIKHKAIERGSLMGCSIDGNTMTYGTSPGLNNGELLARHVRNMDNSLQDSLDLPRGSDERPTIIPVQYETRMAGCLVRGHAYSVTGL	341		
hCAPN9	DFTGGVAEFTIR-----APENFYEILEKALKRGSLLGCFIDT-----RSAES-----EARTPGLIKGHAYSVTGI	261		
hCAPN1	DFTGGVTEWELRK-----APSDLYQIILKALERGSLGCSIDIS-----VLDK-----EATTFKLKVKGHAYSVTGA	279		
hCAPN2	DFTGGIAEWELKK-----PPNLFKIIQKALQKGSLLGCSIDIT-----S-----AADS-----EATTFKLKVKGHAYSVTGA	269		
hCAPN8	DFTGGISEFYDLKK-----PPENLYYIIQKALKRGSLLGCSIDVS-----T-----AAEA-----EATTFKLKVKGHAYSVTGV	269		
hCAPN10	DLTGGLAERWNLKGVAGSGGQDPRGRWEHRTCRQLLHLADQCLISCC-----VLS-----PRAGARELGEFHAIVSDI	245		
hCAPN5	RKVLRLGHLLAFFKSEKLDMLRLNPNWGEREWGMPWSDTSEEQKVSSEKREKMGVTQDDGEFWMTEFEDVCRYPTDIIKCRVINTSHL-SIHKTEWEARL-----HGAWTLHEDPRQNRG	373		
hCAPN6	RKRLRGLERLVEVFSTEKLYMVLRLNPLGRQEWGSGPWEISEEQQQLTVTDNRKMLGLVMSDDGEFWMSEDFCHNFHKLAVCRNVNN-----PVFGRKELESV-----VGCTVDDPLNRS	371		
hCAPN3	DEVFP-----KGEKVLRLNPLGRQEWGSGPWEISEEQQQLTVTDNRKMLGLVMSDDGEFWMSEDFCHNFHKLAVCRNVNN-----PVFGRKELESV-----VGCTVDDPLNRS	371		
hCAPN9	DQVSF-----RGQRIELIRIRNPWQGVWNGSWSDSPEWRSVGPABEQKRLCHTALDDGEFWMSEDFCHNFHKLAVCRNVNN-----PVFGRKELESV-----VGCTVDDPLNRS	444		
hCAPN1	KQVNY-----RGQVVSILIRNPNWGEVWNTGAWSDSSSEWNNVDPYERDQLRVKME-DGEFWMSEDFCHNFHKLAVCRNVNN-----PVFGRKELESV-----VGCTVDDPLNRS	364		
hCAPN2	EEVES-----NGSLQKLIIRNPNWGEVWNTGAWSDSSSEWNNVDPYERDQLRVKME-DGEFWMSEDFCHNFHKLAVCRNVNN-----PVFGRKELESV-----VGCTVDDPLNRS	381		
hCAPN8	EEVNF-----HGRPEKLIIRNPNWGEVWNTGAWSDSSSEWNNVDPYERDQLRVKME-DGEFWMSEDFCHNFHKLAVCRNVNN-----PVFGRKELESV-----VGCTVDDPLNRS	371		
hCAPN10	RELQG-----QAGQCILLRLIQNPWGRRCWGLWRREGGEGNSQVDAAVASELLSQLQ-EGEFWVEEEFREFDELTVGYPTVEAGHLQSLTERLLCHTRALPGAWVKG-----QSA	352		
hCAPN5	GGCINHKDTFFQNPQYIFEVKKPED-----EVLICIQQRPKSTRREGKGENLAIGFDIYKVE-----E-----NRQYRMHSL-----QHKAASSIYNSRVFLRTDQPEGRVLIPT	472		
hCAPN6	GGCYNRRDTFLQNPQYIFTEVDEGH-----KVLMSLQKDLRTYRRMGRPDNYIIGFELFKVE-----M-----NRFRHLHLYIQRAGTSTYIDTRTVFLSKYLKKGSYVLNPT	472		
hCAPN3	GGCRNFPDFTWNPQYRLKLEEDD-----DPPDSEV-ICSFVLALMQRNRKDRKLG-ASLFTIGFAIYEVPEKMHGK-CHLQKDFFLYNASKARSKTYINREVSQRFRLPPSEYIVPS	559		
hCAPN9	GGCRNFLTFTWNPQYRLKLEEDD-----DPPDSEV-ICSFVLALMQRNRKDRKLG-ASLFTIGFAIYEVPEKMHGK-CHLQKDFFLYNASKARSKTYINREVSQRFRLPPSEYIVPS	471		
hCAPN1	GGCRNYPATFWNPQYRLKLEEDD-----DPPDSEV-ICSFVLALMQRNRKDRKLG-ASLFTIGFAIYEVPEKMHGK-CHLQKDFFLYNASKARSKTYINREVSQRFRLPPSEYIVPS	499		
hCAPN2	GGCRNYPNTFWNPQYRLKLEEDD-----DPPDSEV-ICSFVLALMQRNRKDRKLG-ASLFTIGFAIYEVPEKMHGK-CHLQKDFFLYNASKARSKTYINREVSQRFRLPPSEYIVPS	487		
hCAPN8	GGCLNYPGTWNPQYRLKLEEDD-----DPPDSEV-ICSFVLALMQRNRKDRKLG-ASLFTIGFAIYEVPEKMHGK-CHLQKDFFLYNASKARSKTYINREVSQRFRLPPSEYIVPS	489		
hCAPN10	GGCLNYPNPFQYRLKLEEDD-----DPPDSEV-ICSFVLALMQRNRKDRKLG-ASLFTIGFAIYEVPEKMHGK-CHLQKDFFLYNASKARSKTYINREVSQRFRLPPSEYIVPS	471		
hCAPN5	TFEPHGTGEFLRLVFTDVPNSCRELRLEPPHT-----C-----WSSLCGYPQLVTQVHVLAAGLKD-----530			
hCAPN6	MFQHGRTSEFLRLVFTDVPNSCRELRLEPPHT-----C-----WSSLCGYPQLVTQVHVLAAGLKD-----532			
hCAPN3	TFEPHGTGEFLRLVFTDVPNSCRELRLEPPHT-----C-----WSSLCGYPQLVTQVHVLAAGLKD-----532			
hCAPN9	TFEPHGTGEFLRLVFTDVPNSCRELRLEPPHT-----C-----WSSLCGYPQLVTQVHVLAAGLKD-----532			
hCAPN1	TFEPHGTGEFLRLVFTDVPNSCRELRLEPPHT-----C-----WSSLCGYPQLVTQVHVLAAGLKD-----532			
hCAPN2	TFEPHGTGEFLRLVFTDVPNSCRELRLEPPHT-----C-----WSSLCGYPQLVTQVHVLAAGLKD-----532			
hCAPN8	TFEPHGTGEFLRLVFTDVPNSCRELRLEPPHT-----C-----WSSLCGYPQLVTQVHVLAAGLKD-----532			
hCAPN10	TFEPHGTGEFLRLVFTDVPNSCRELRLEPPHT-----C-----WSSLCGYPQLVTQVHVLAAGLKD-----532			
hCAPN5	-----SPTGANSYVIIKCEGDKVRSAVQKG-----TSTPEYNVKGIFYRKKLSQPIITQVWNR-----VLKDFELGQVHLKADPNDLQALHTLHLDRNSRQ	618		
hCAPN6	-----ANETVNPYLIIOGKEEVRSPVQKN-----TVHAIPTDQAIYRRTTIDIPIIQVWNR-----KFCDFQGLQVTLADPNSDCRDLKSLYLKKGKGT	620		
hCAPN3	VVNKKDLKTHGFTLESCRSMLADTDGSGKLNQEFHHLNKKIKAWQKIFKHYYDQSGTINSYEMRANVNDAGFHLNQLYDITIMRYADKHMINDFDSFICCFVRLBGFRAFHAF	799		
hCAPN9	VLQKKDKIKFKKLSLISCKNIIISLMDTSGNGKLEFDEFKVFWDKLGQWNLFLRFDADKSGTMYELRTALKAAQFQLSSHLQLVILRYADEELQDFDDFLACLVRLENASRVFQAL	668		
hCAPN1	IISKHDLRTKGFSLSCRSVNLNDRDNGKLGLEFVFNILNIRNYLSIFKFDLQKSGMSAYEMHMAIESAGFKLAKKLYELIITRYSEPDLAVDFDNFVCLVRLETFRFFKTL	692		
hCAPN2	VLAKRQDKISDGFSTETCKIMVMDLSDGSGKLGKEFYILWTKIQYQKIYREIDVDRSGTMSYEMRANVNDAGFHLNQLYDITIMRYADKHMINDFDSFICCFVRLBGFRAFHAF	679		
hCAPN8	VLAKRQDKISDGFSTETCKIMVMDLSDGSGKLGKEFYILWTKIQYQKIYREIDVDRSGTMSYEMRANVNDAGFHLNQLYDITIMRYADKHMINDFDSFICCFVRLBGFRAFHAF	682		
hCAPN10	PCFPFVPEGPGPRCVRITLHQHCRPSD-----TEFHPIGFHFQVPEGGRSQDAPLLQLQEPILSCVPHRYAQEVSRCLLPLAGTYKVPSTYLPDTBGAFTVTIATRIDRPSIHSQ	654		
hCAPN5	PSNLPGTVAVHILSSTSLMAV-----639			
hCAPN6	AKVKQGHISFKVISSDDLT-----641			
hCAPN3	DKDQGGIILNVLNLEWLQTHYA-----821			
hCAPN9	STKNKEFIHLNINEFIIHLMNI-----690			
hCAPN1	DTDLGQVVTDFLKKLQTHYA-----714			
hCAPN2	DPENTGTIELDLISWLCFSVL-----700			
hCAPN8	DKDQNGIVQLSLAENLCCVLV-----703			
hCAPN10	EMLGQFLQEVSVMAVMKT-----672			

FIG. 5

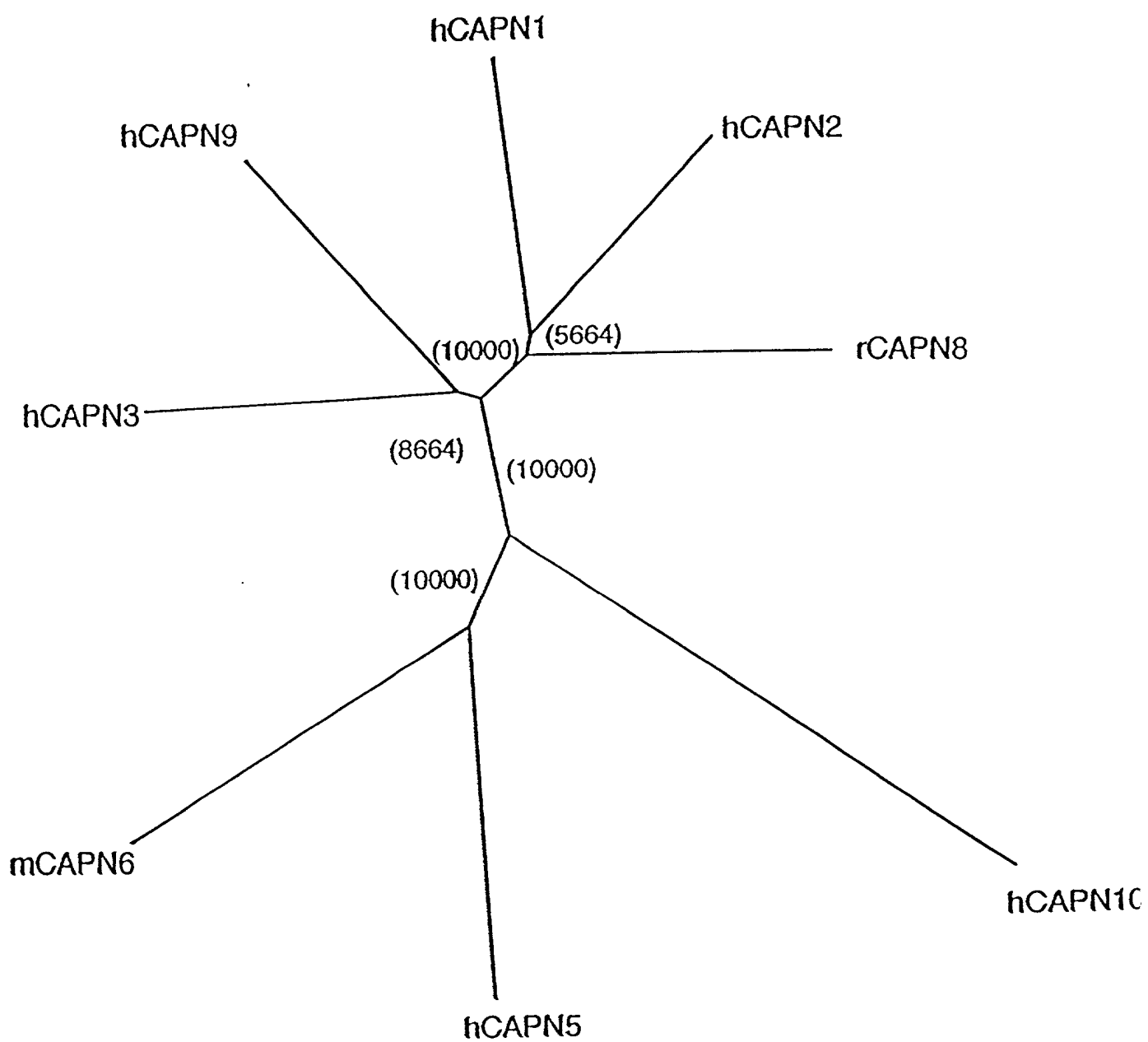


FIG. 6

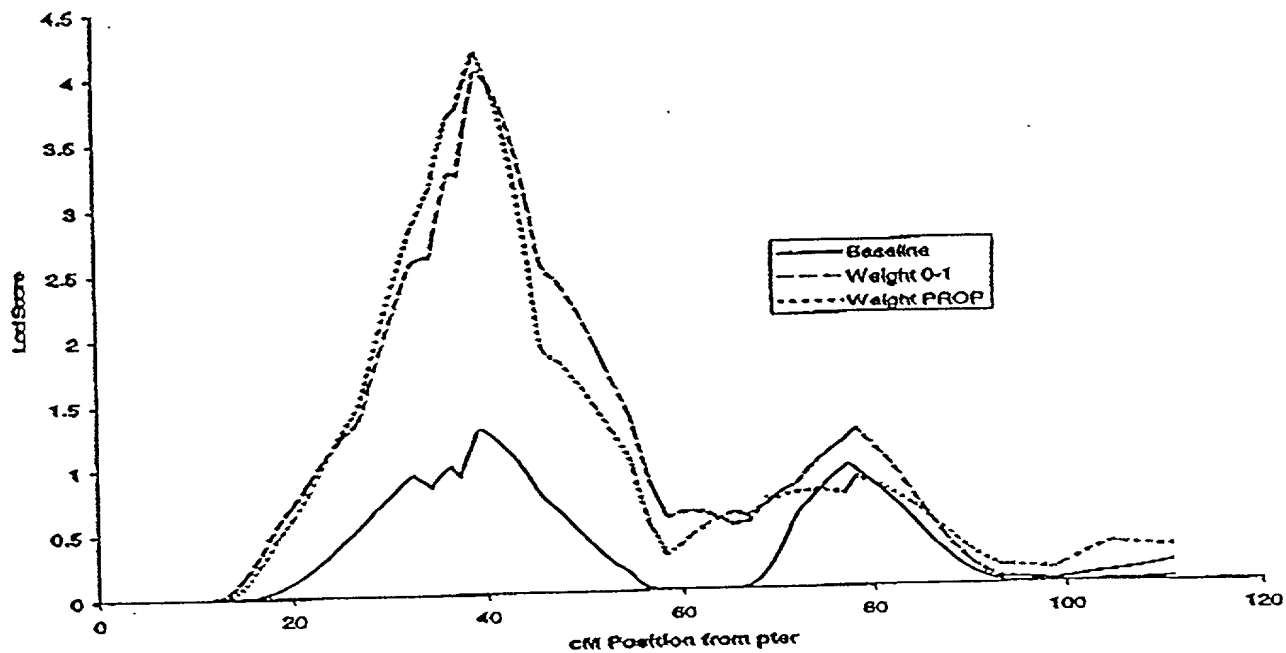


FIG. 7A

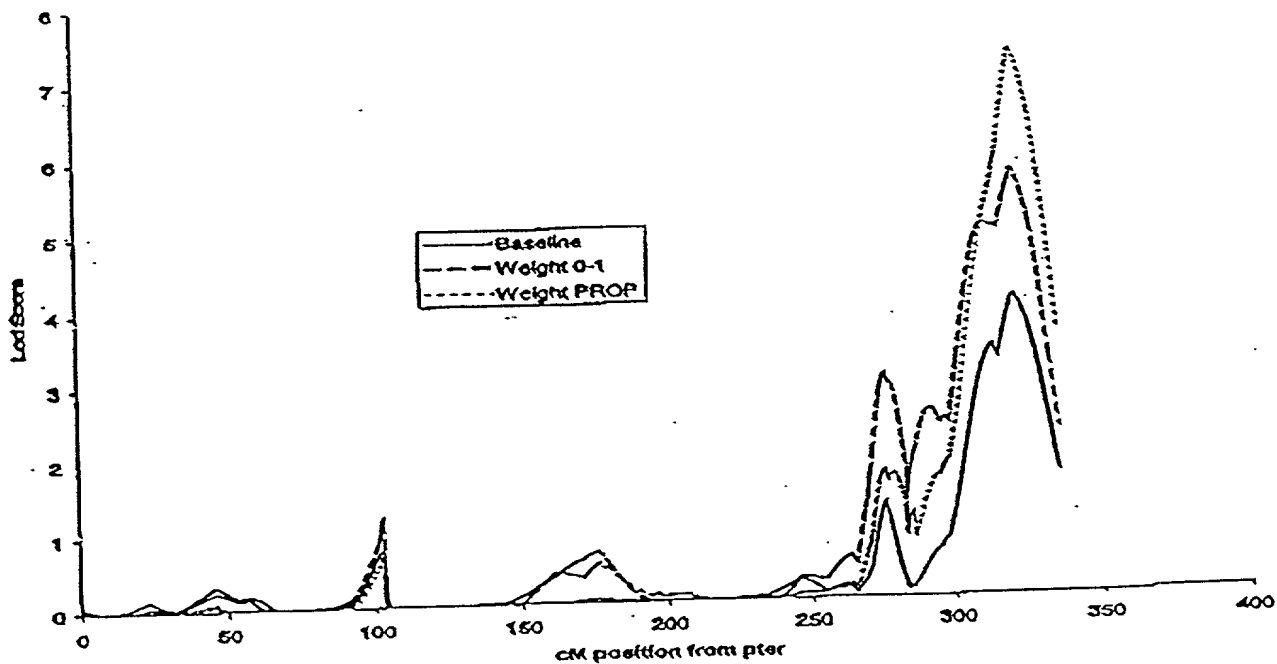


FIG. 7B

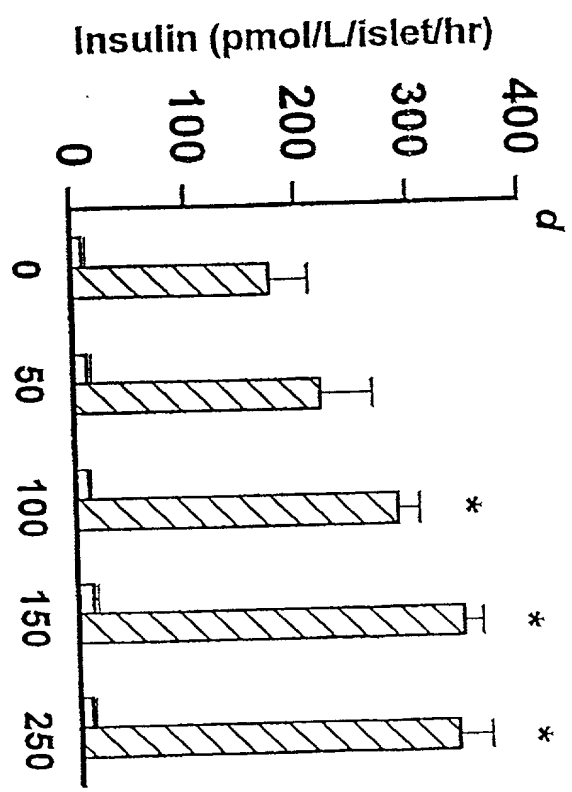
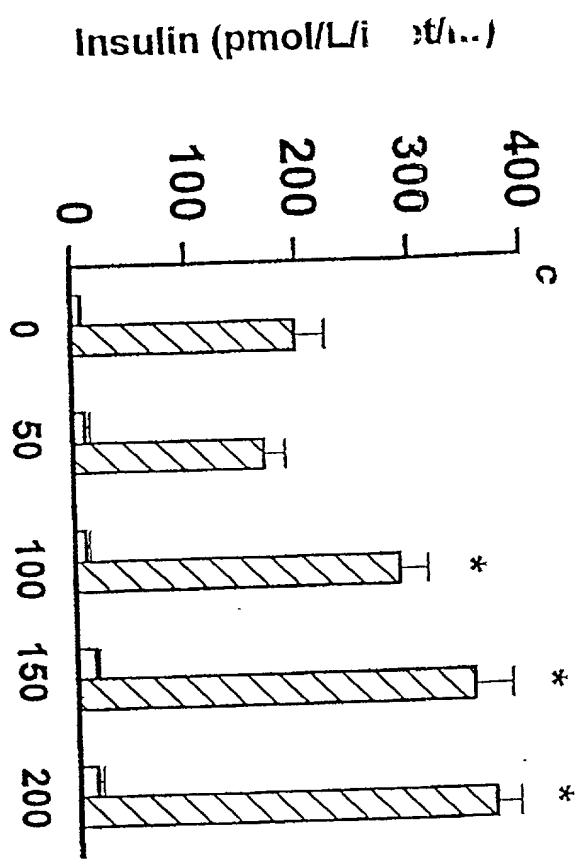
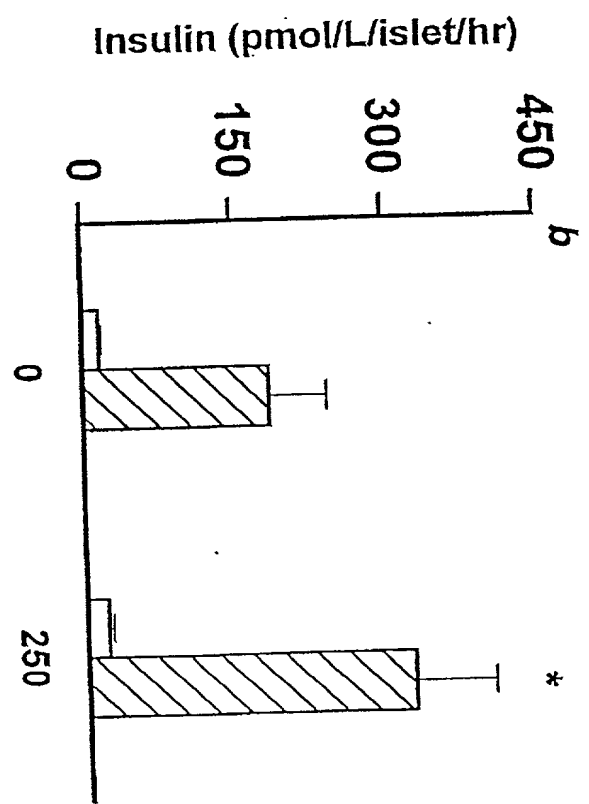
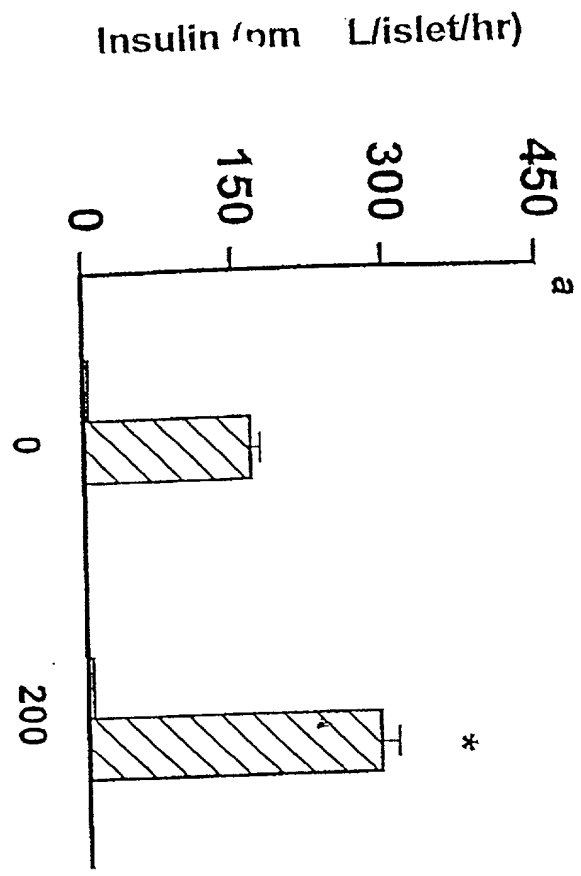


FIG. 8

FIG. 8 shows the effect of increasing concentrations of islet/hr on insulin secretion. The y-axis represents insulin concentration in pmol/L/islet/hr. The x-axis represents islet/hr concentration. The data shows that insulin secretion increases with increasing islet/hr concentration, and is significantly higher at 100, 150, and 200 pmol/L/islet/hr compared to 0 and 50 pmol/L/islet/hr.

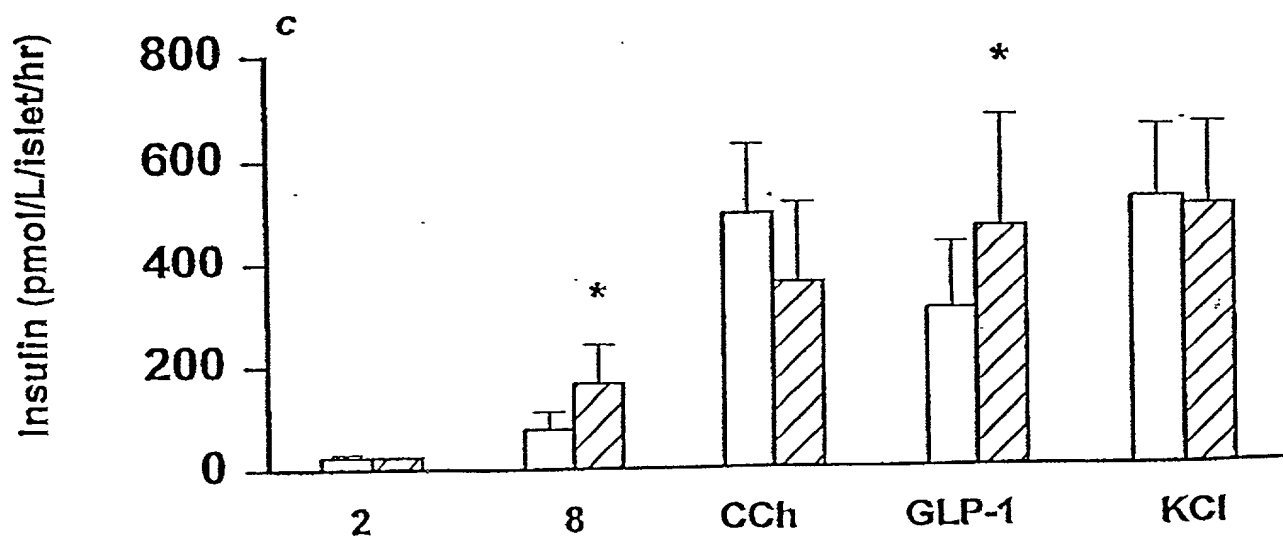
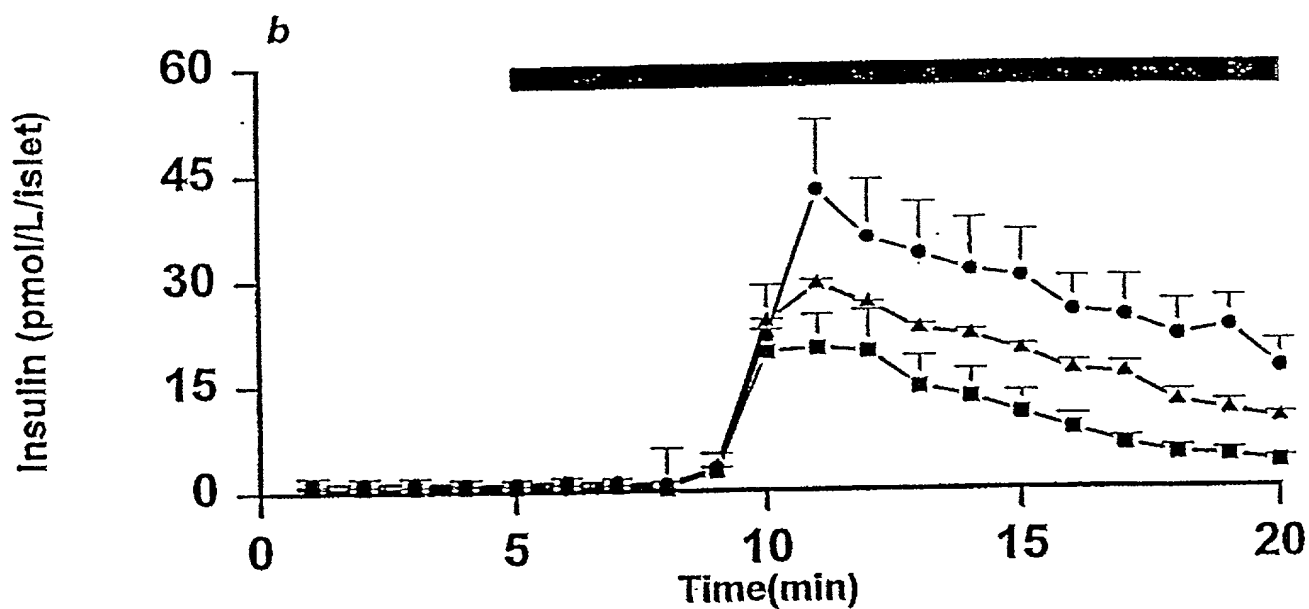
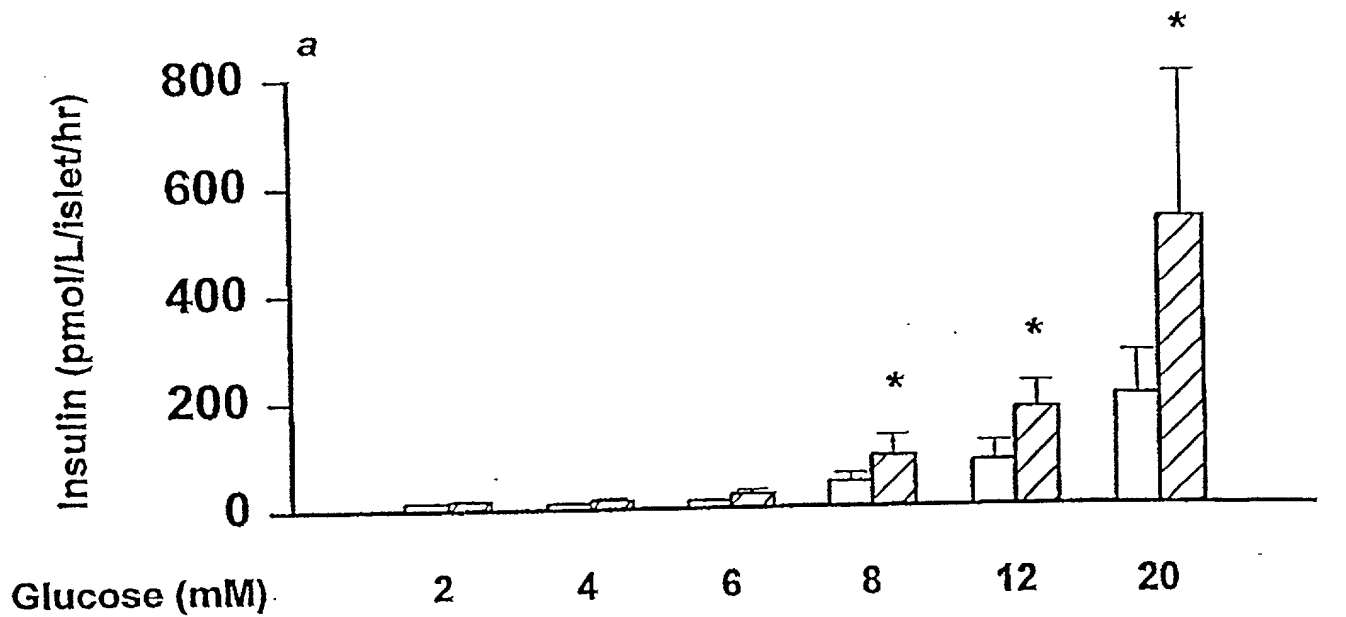


FIG. 9

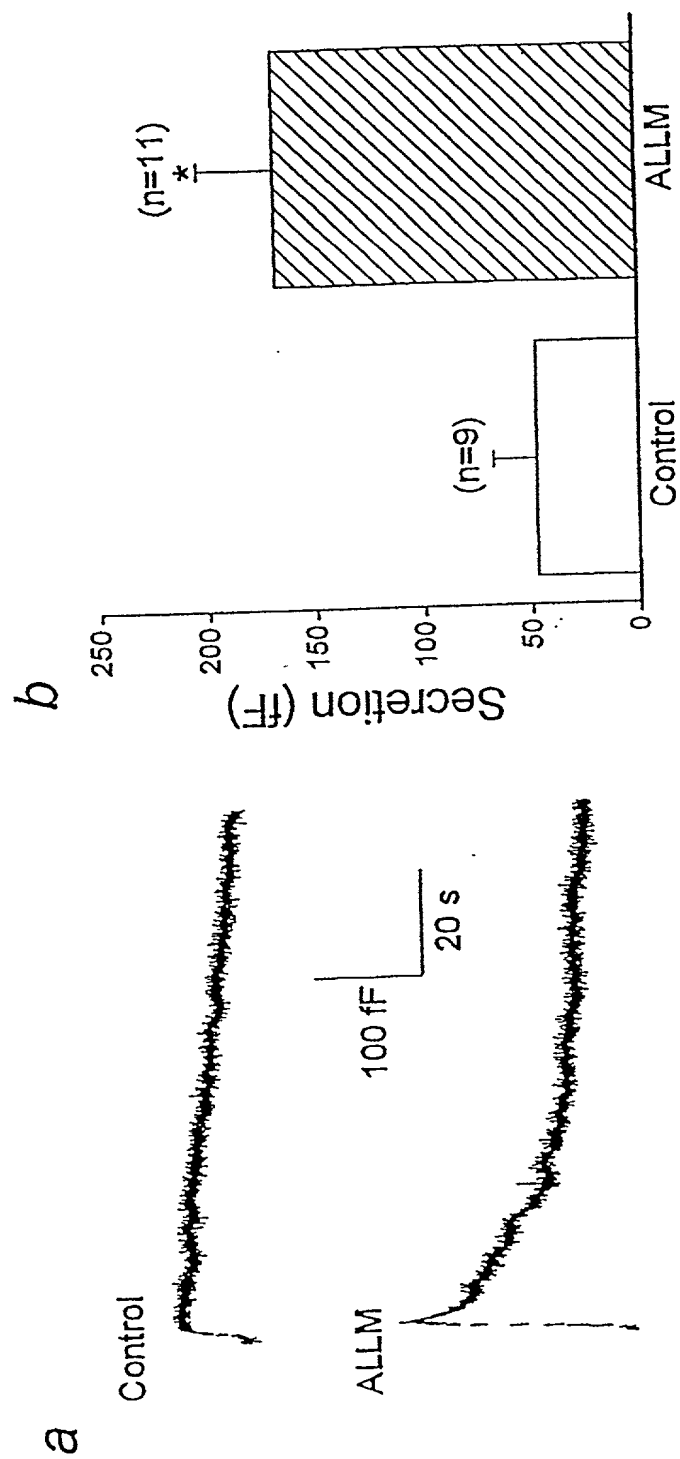


FIG. 10

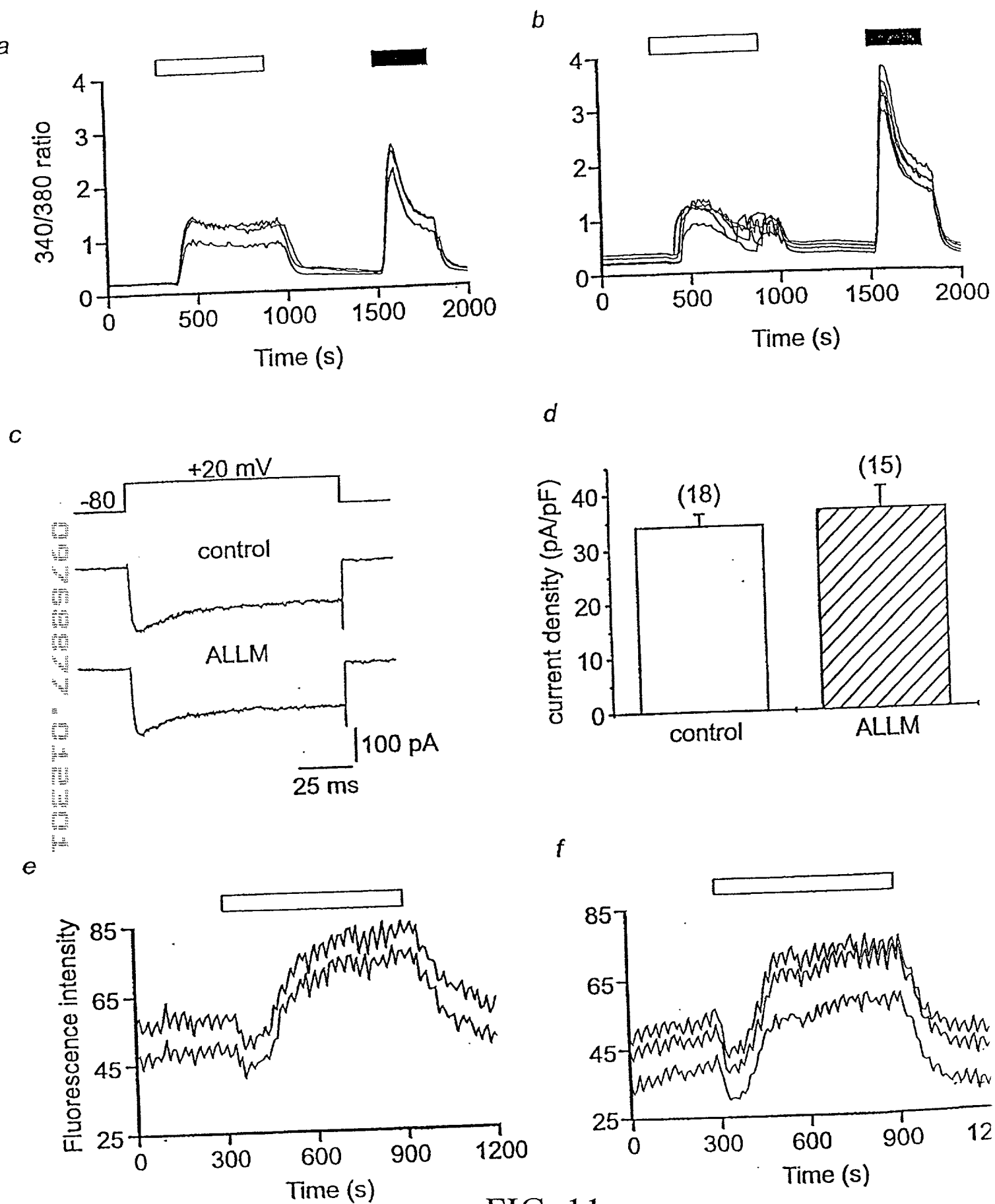


FIG. 11

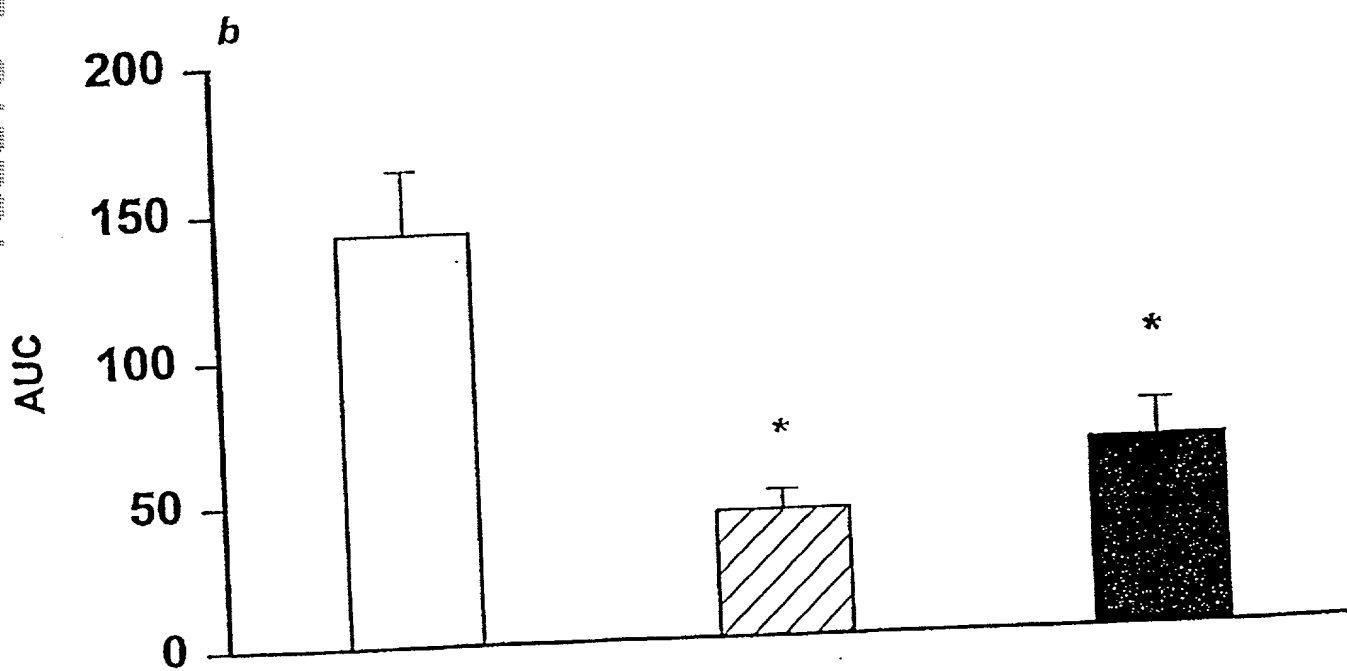
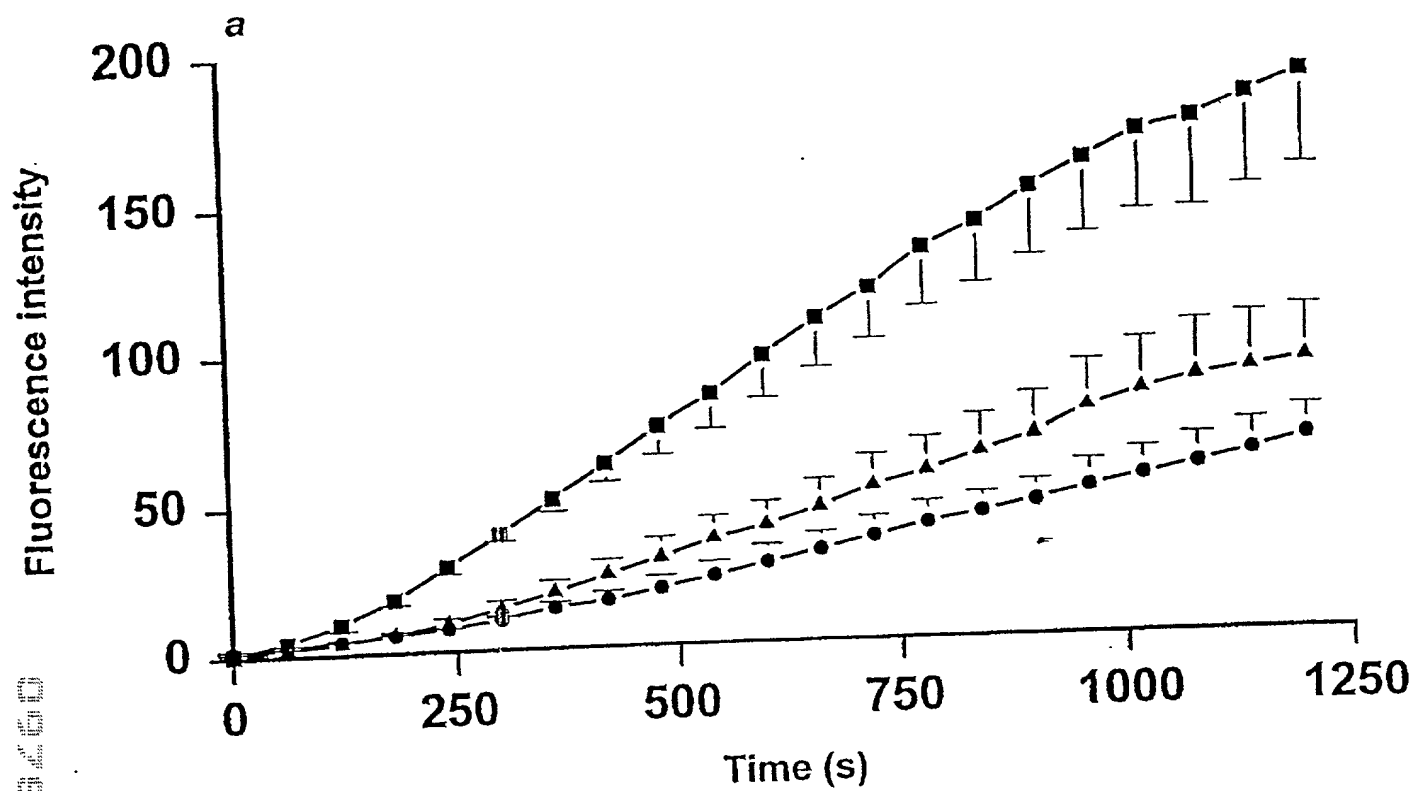


FIG. 12

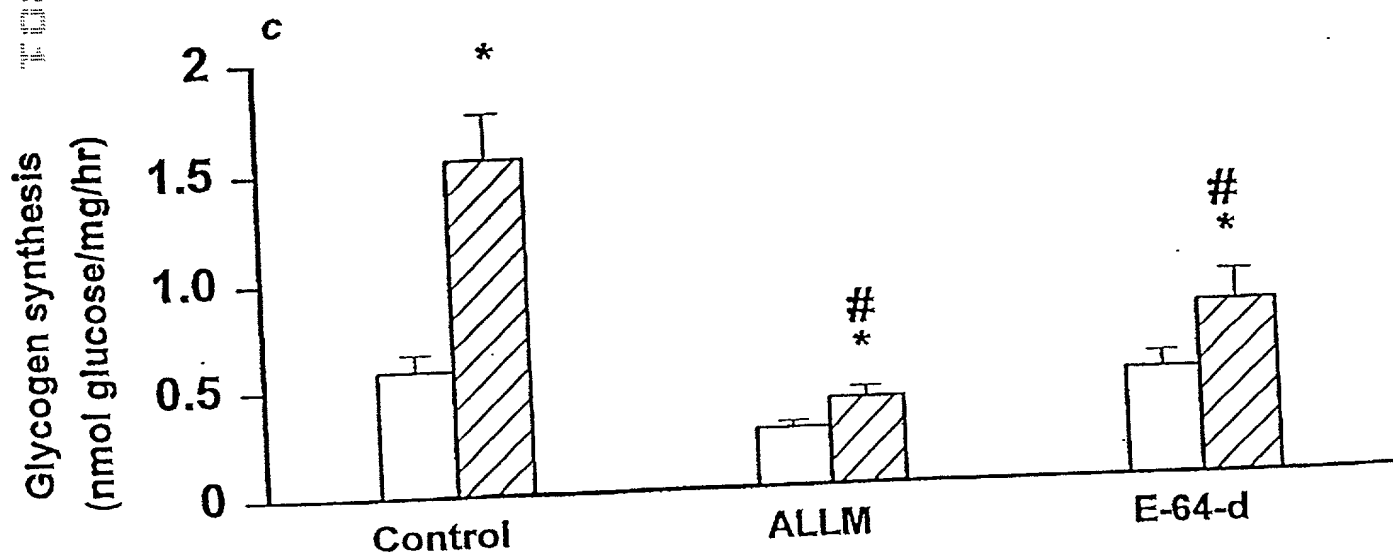
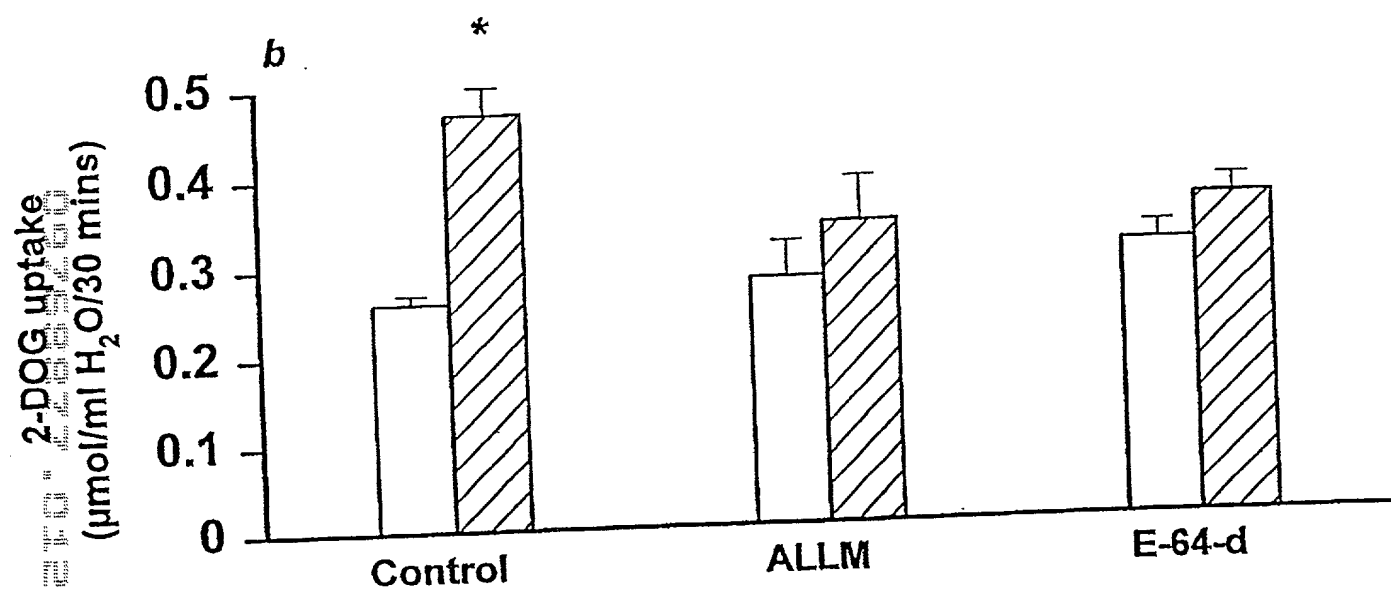
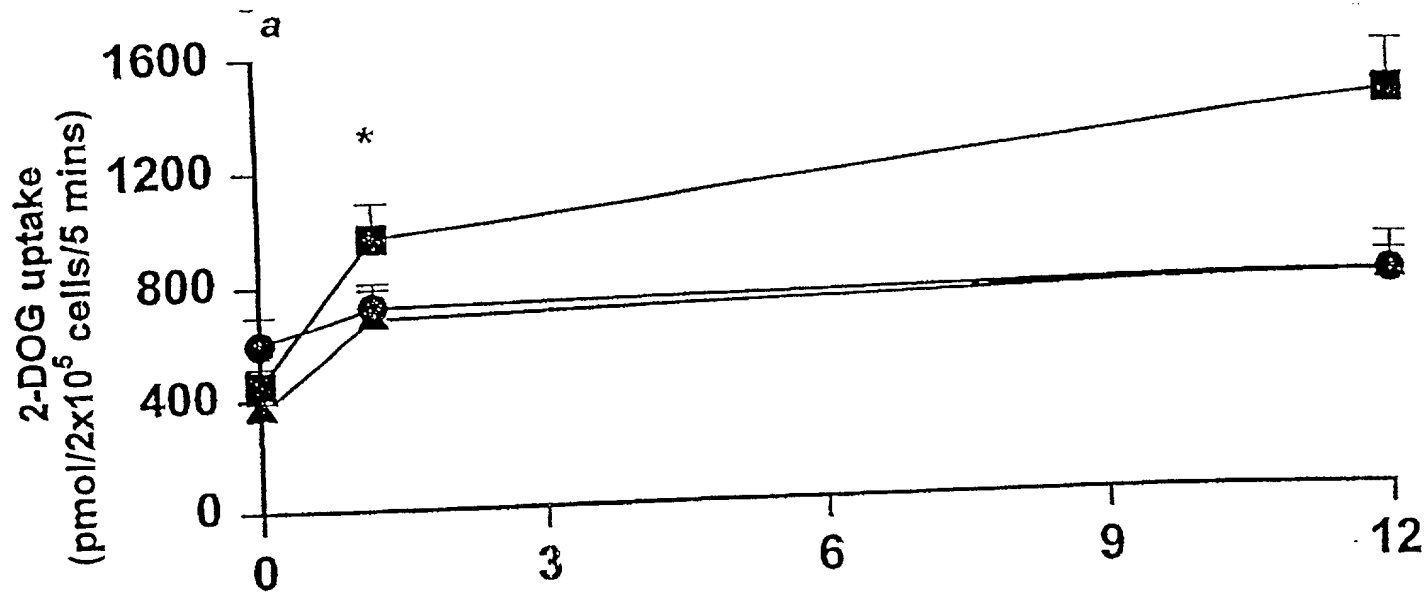


FIG. 13

Fig14. Effect of 48 hours exposure of islets to calpain inhibitors on insulin secretion

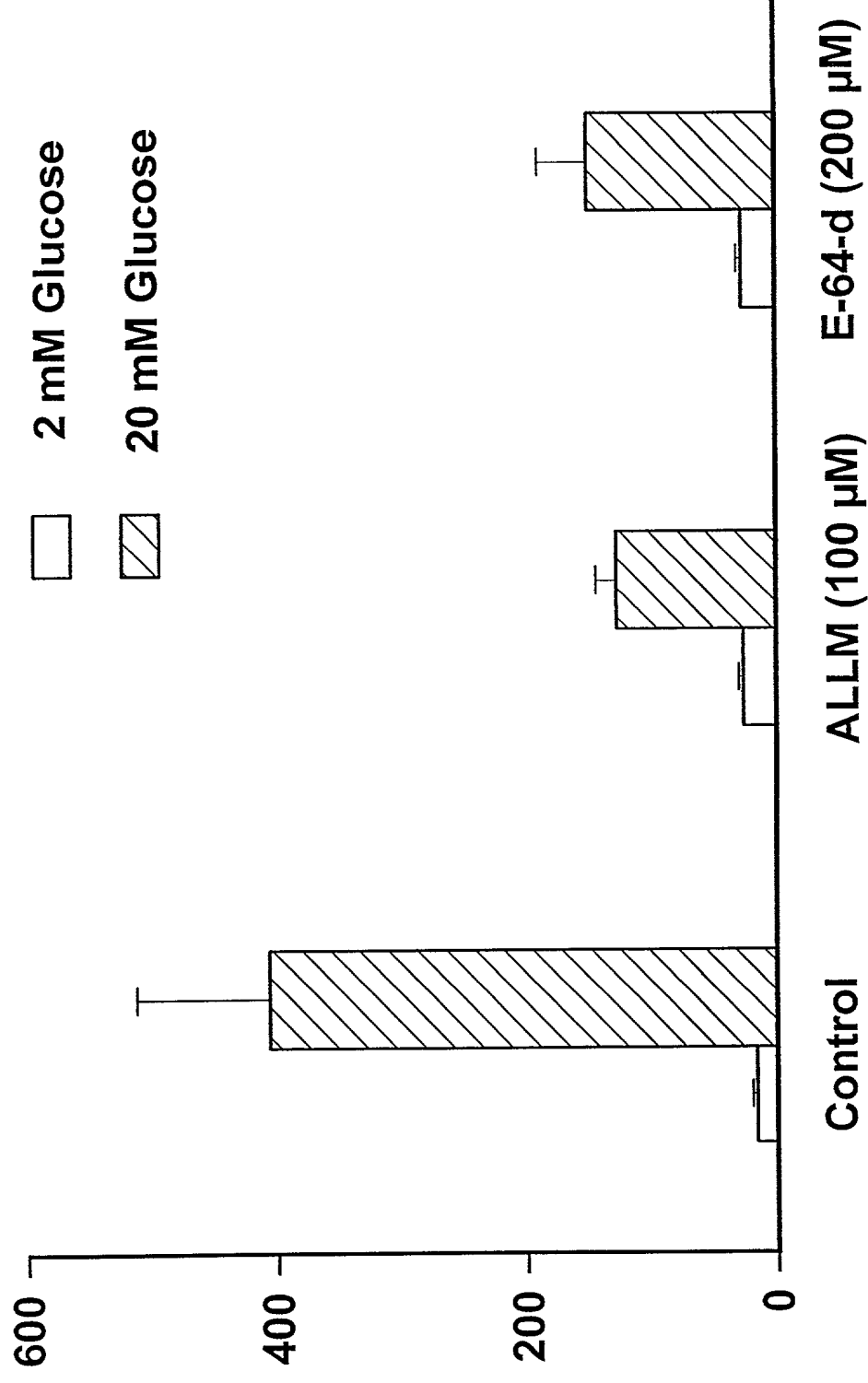


Fig 15 Insulin content in 48 hour cultured islets (n=4)

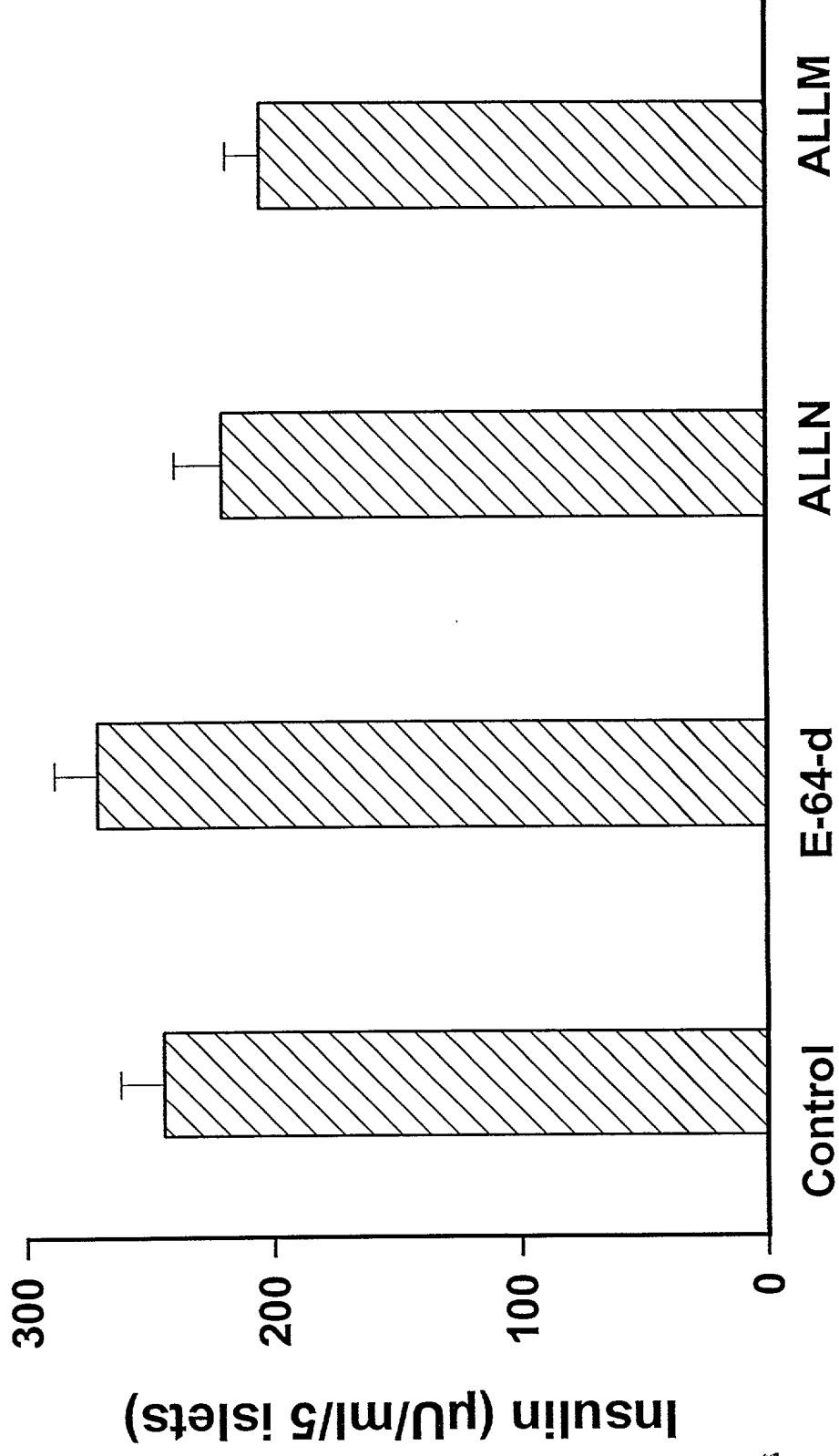


Fig16. ALLM dose response in 48 hour treated islets

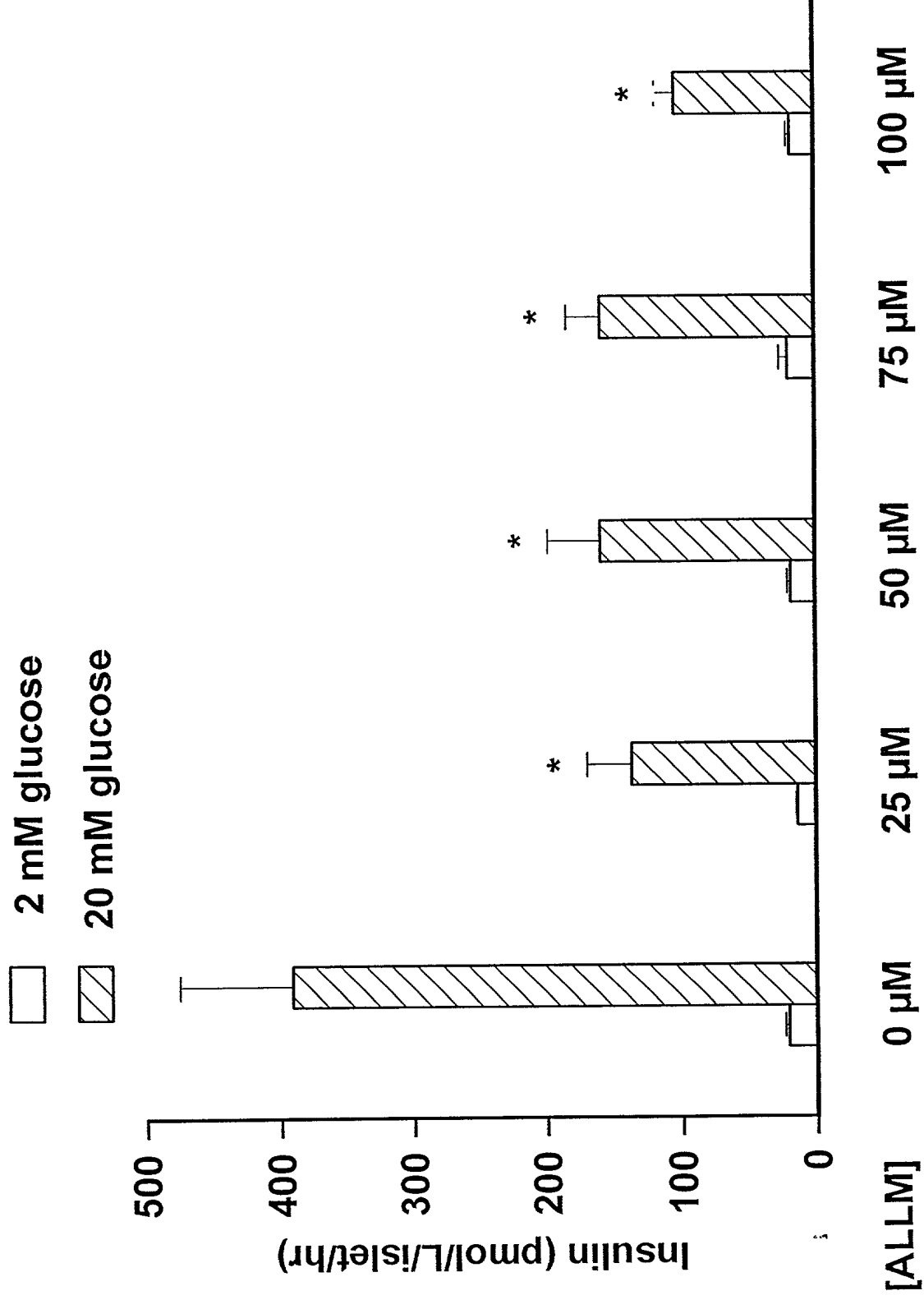
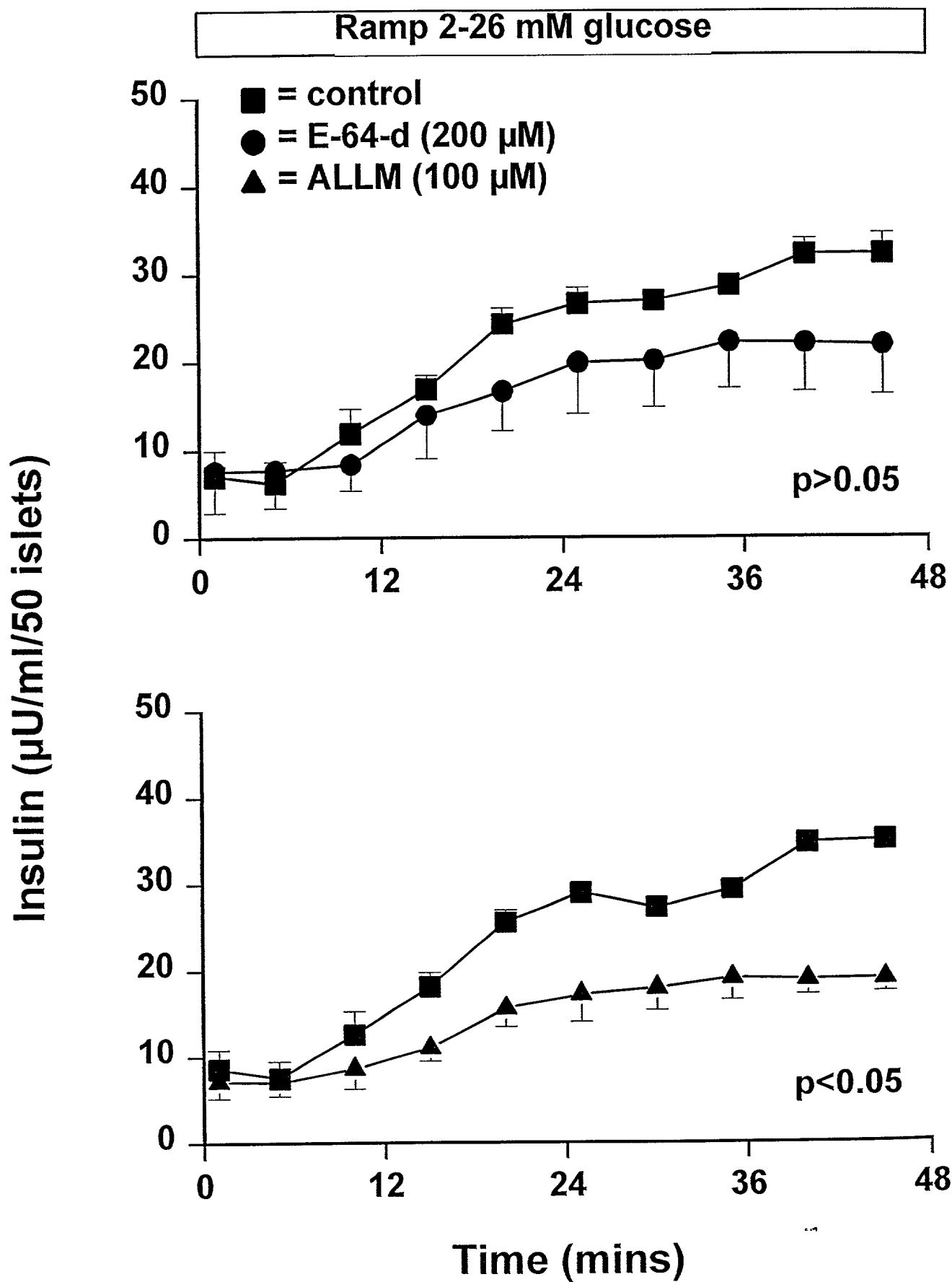


Fig17. Perifusion of 48 hour cultured islets (n=4)

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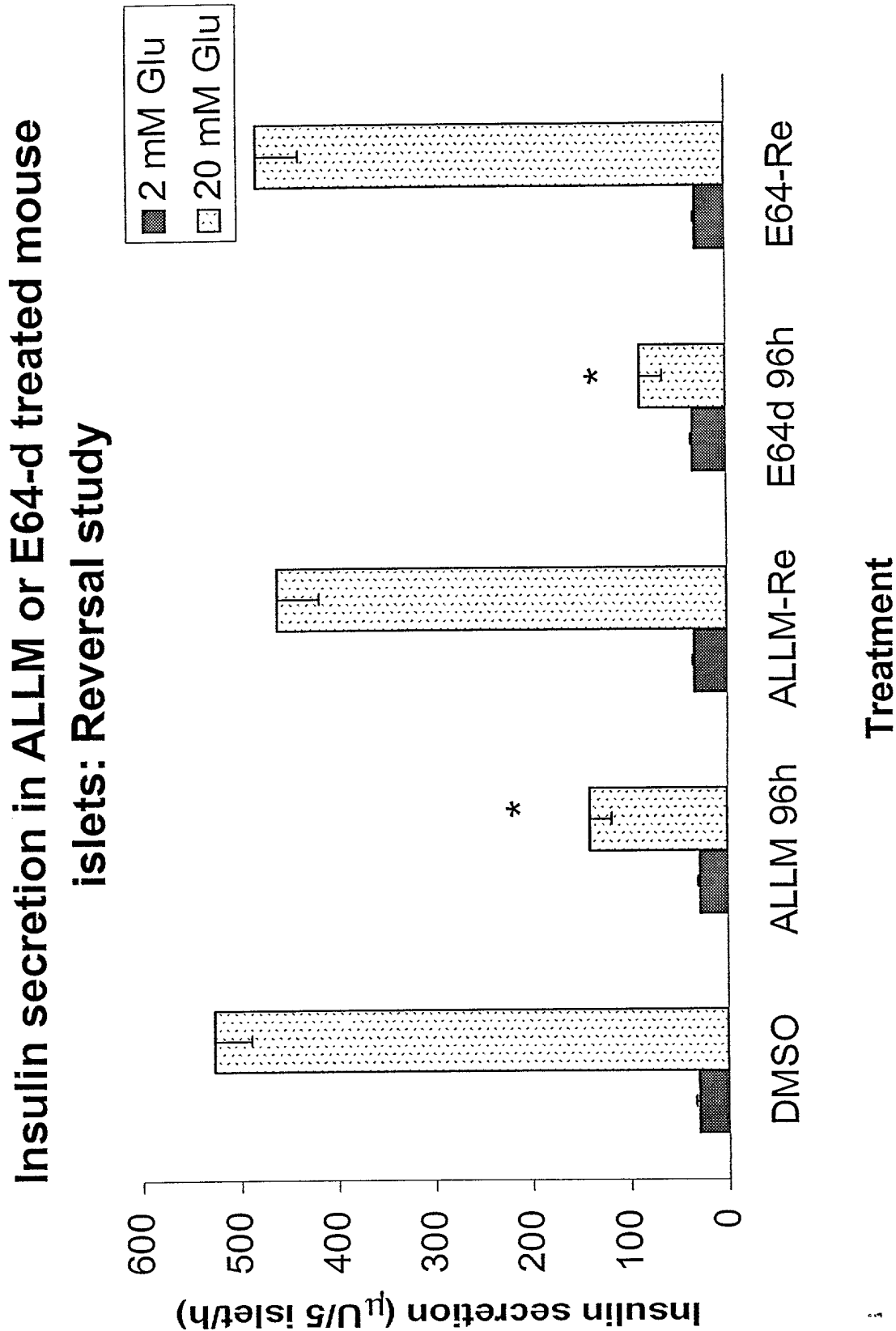
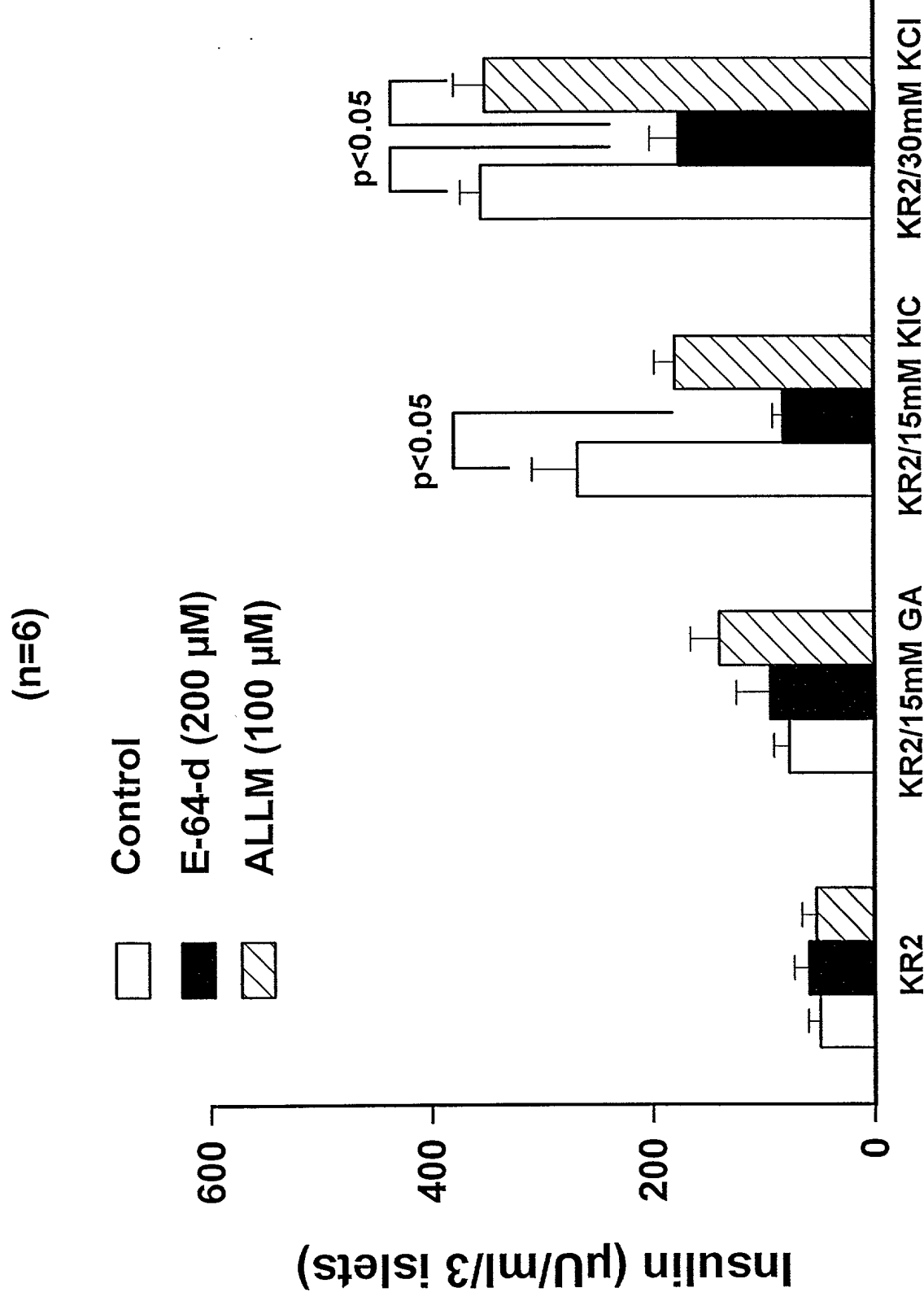


Fig. 18

Fig19. Insulin secretion by islets following exposure to calpain inhibitors for 48 hrs



Mastoparan-induced insulin secretion: Effects of calpain inhibitor

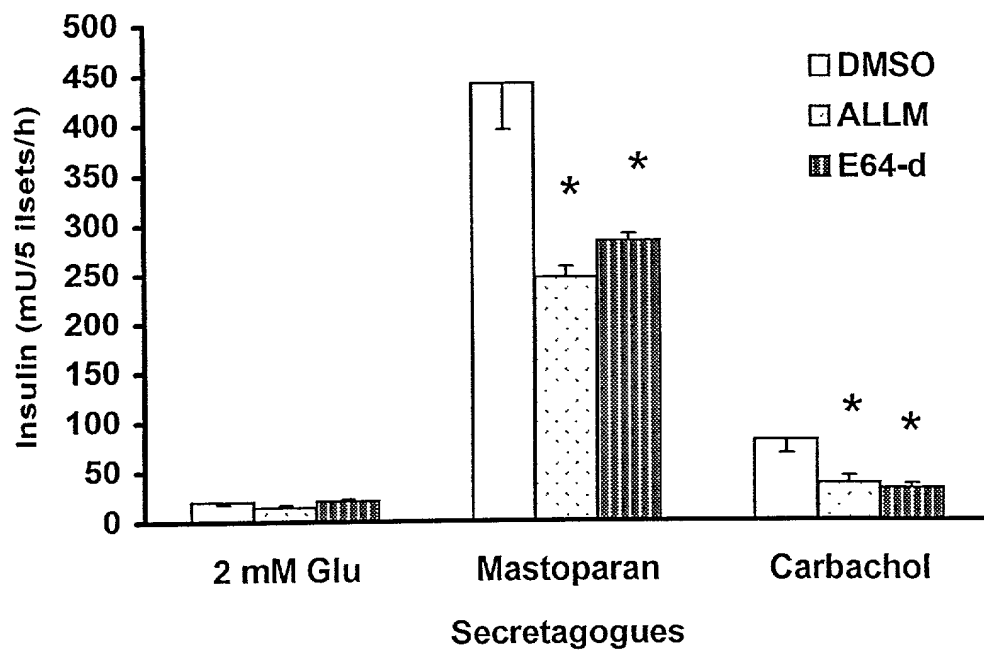
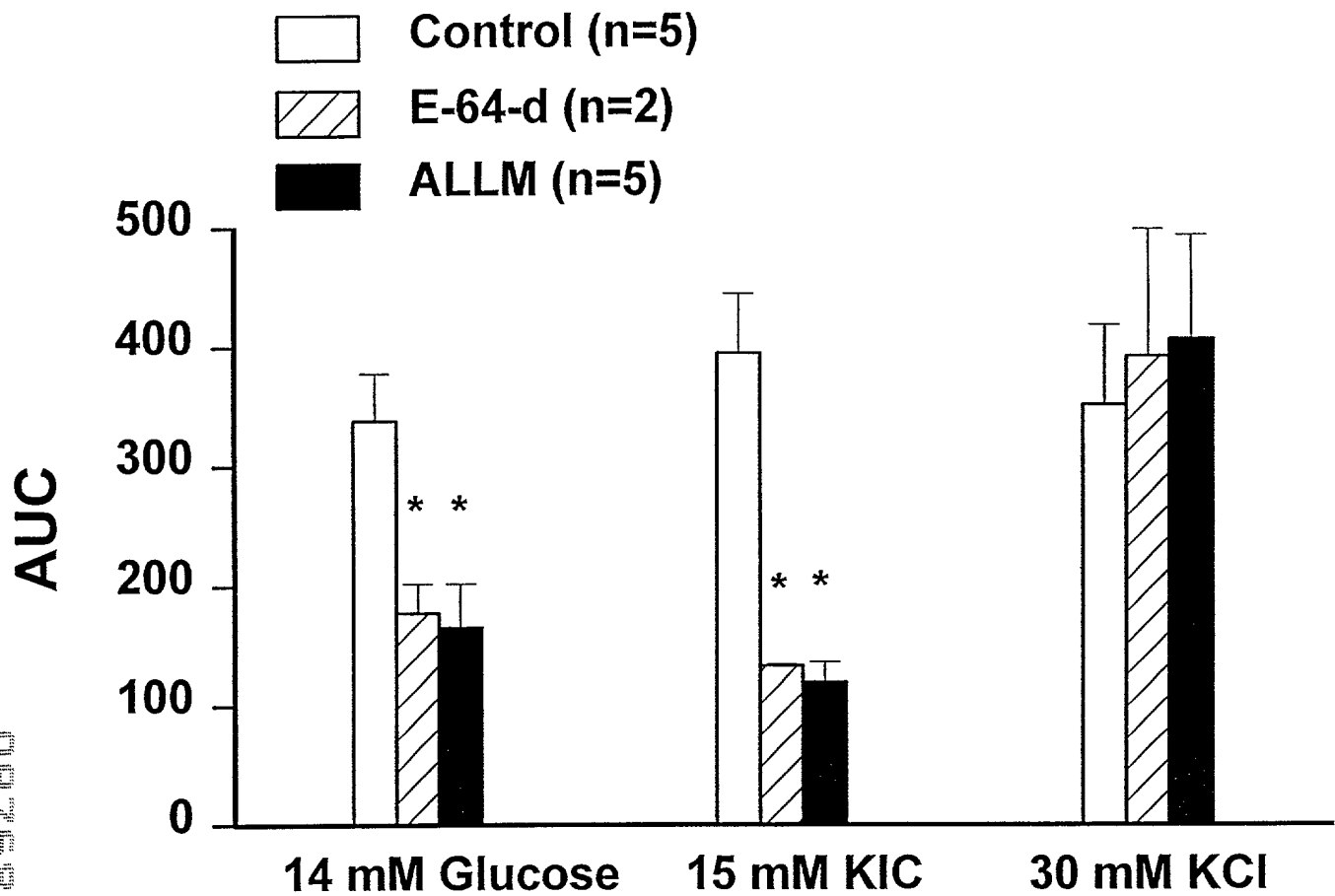
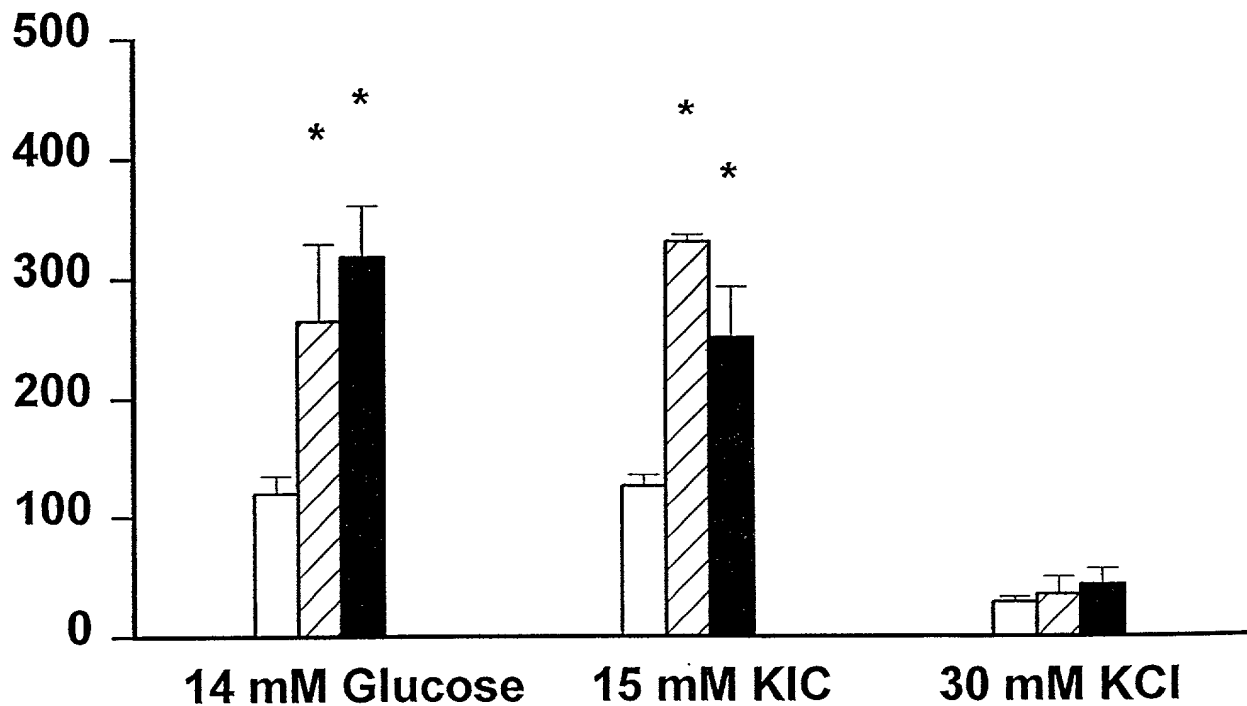


FIG. 20

Fig 21. $[C^{2+}]_i$ responses to glucose, KIC and KCl



Time to 1/2 max response (s)



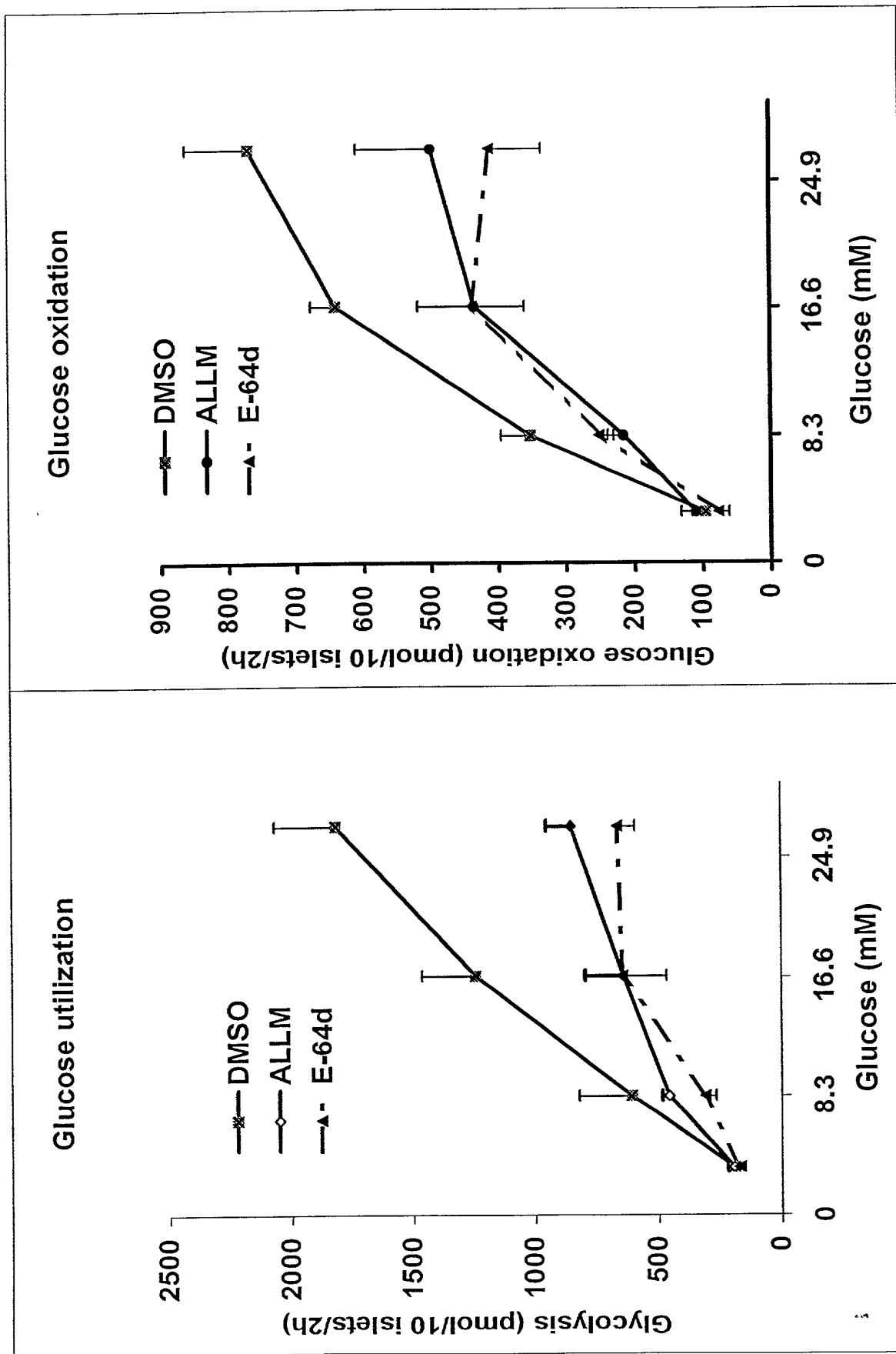
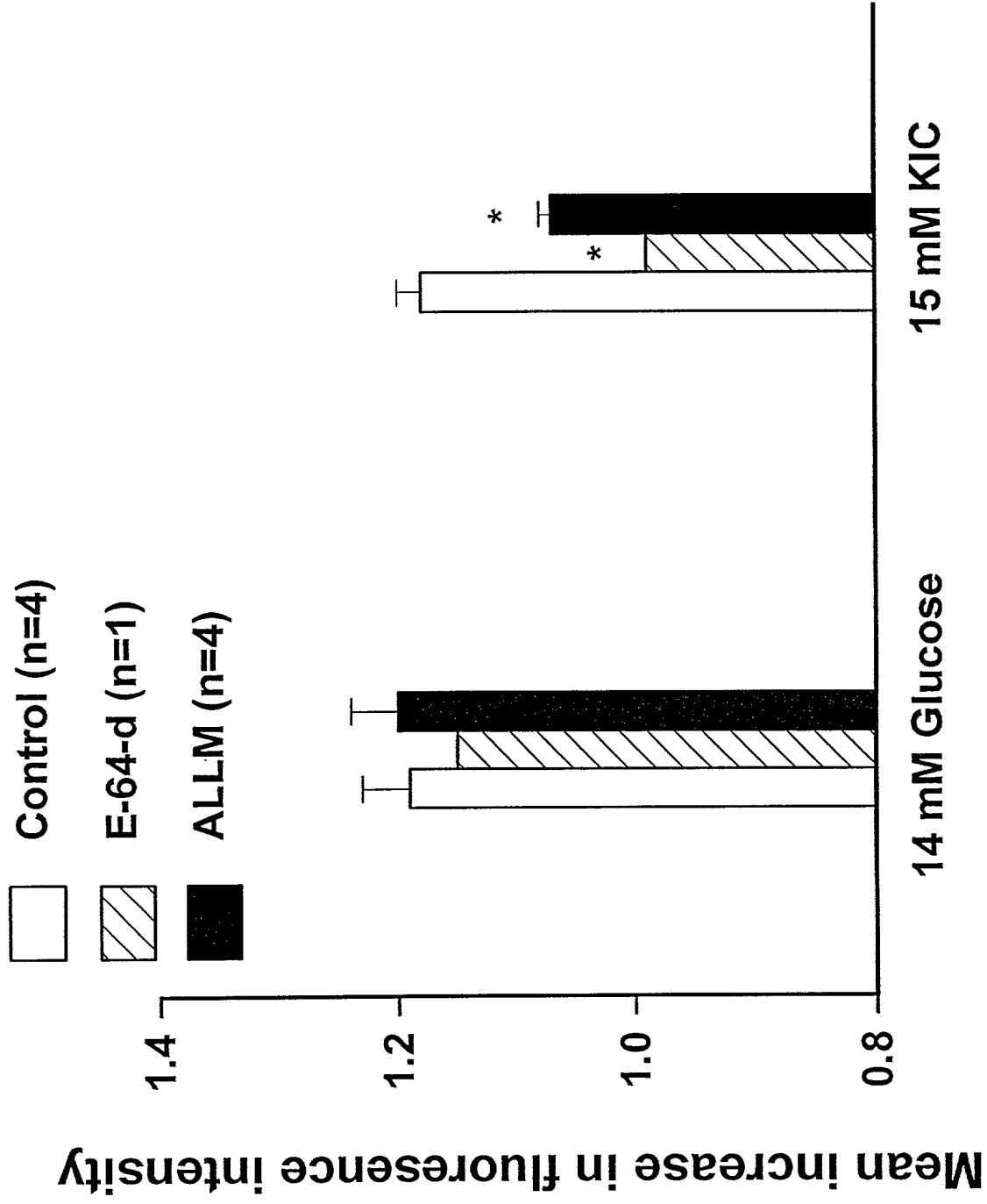


Fig. 22

Fig 23. NAD(P)H responses to glucose and KIC



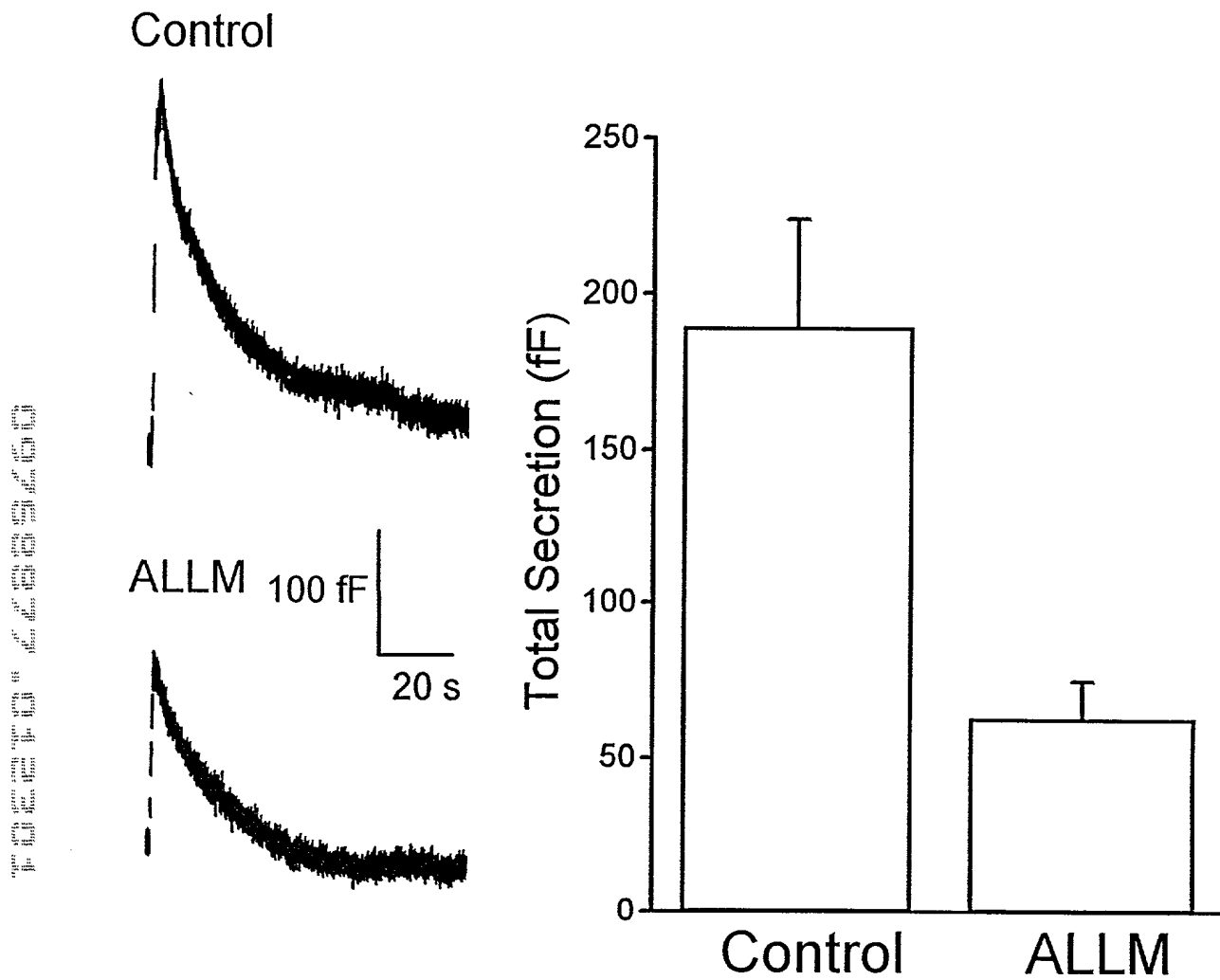


Fig. 24. Measurement of membrane capacitance in isolated β -cells

A black and white photograph of a dense forest. Sunlight filters through the canopy, creating bright, circular highlights on the dark, textured ground and foliage. The image has a grainy, high-contrast quality, typical of older film photography.

[illegible]

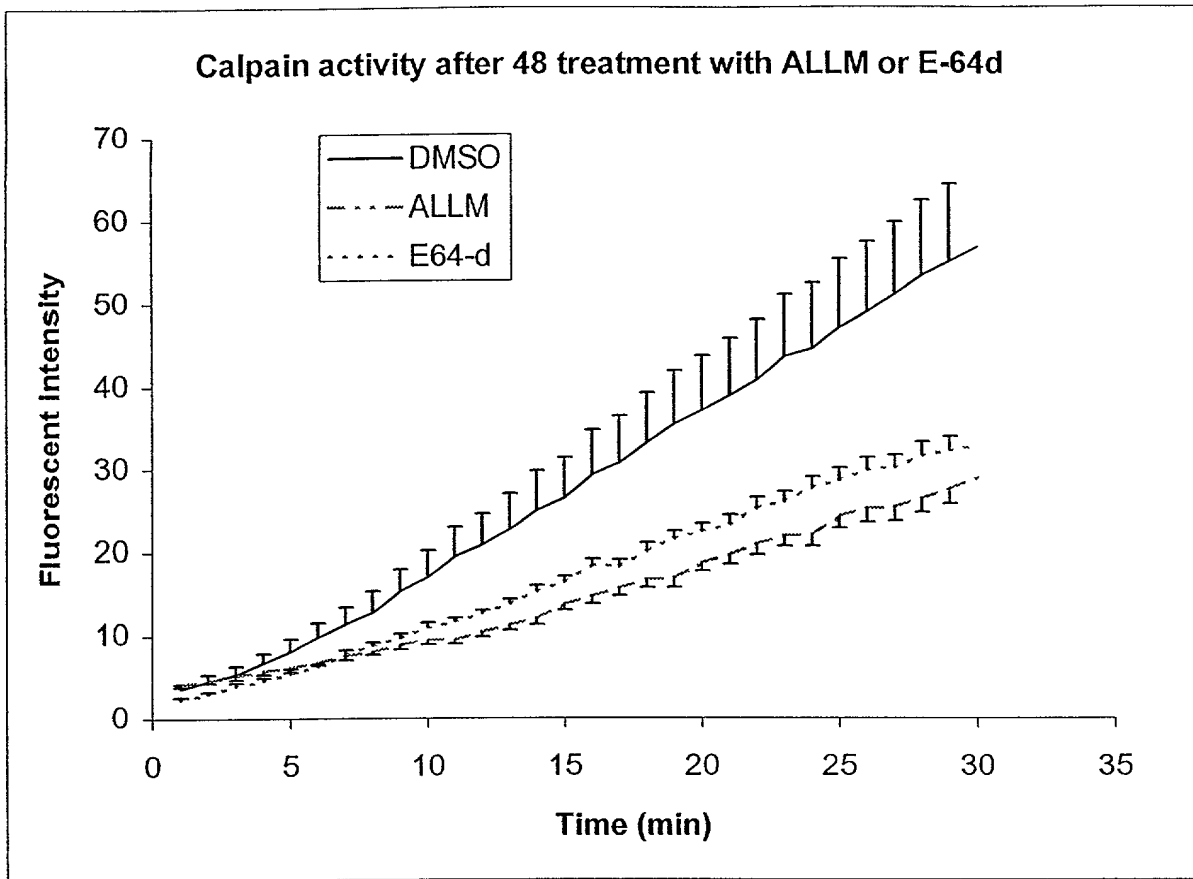


FIG. 26